The American Heart Journal

VOL. 13 APRIL, 1937 NO. 4

Original Communications

AN ORTHODIAGRAPHIC STUDY OF 291 COLLEGE STUDENTS WHO SHOWED NO EVIDENCE OF HEART DISEASE*

JOSEPH EDEIKEN, M.D., AND FRANCIS CLARK WOOD, M.D.
PHILADELPHIA, PA.

THE material comprising this study consists of the orthodiagrams of 291 male college students between the ages of sixteen and twenty-six years, in whom history, physical examination, and electrocardiographic study showed no evidence of heart disease. Two hundred ninety-nine individuals were examined, but eight were excluded: four, because a tendency to faint precluded accurate orthodiagraphy; and four, because they were found to have heart disease: one showed a congenital lesion, and three had aortic insufficiency. This paper contains a presentation of figures obtained for the various orthodiagraphic measurements in this group; a comparison of them with the generally accepted standards of Eyster and Hodges,[1] a description of the deviations from these standards which were encountered, and a discussion of the adequacy of the orthodiagraphic method for determining pathological cardiac enlargement.

Orthodiagrams were made by the usual technic. They were all done by one of us (J. E.). After completing the upper and lower borders, the area of the silhouette was measured by planimeter. The transverse diameter, cardiothoracic ratio, and anteroposterior diameter were also determined.

Cardiac area was measured in 290 cases† (Fig. 1). In 227 (78.3 per cent) the area was 5 per cent or more below the predicted value. In 172 (59.3 per cent) it was 10 per cent or more below the predicted value. The smallest heart was 28.3 per cent below the predicted figure. On the other hand, only nine students (3.1 per cent) had

*From the Edward B. Robinette Foundation, Medical Clinic, Hospital of the University of Pennsylvania, and from the Department of Student Health, University of Pennsylvania.

†In one case predicted values were not calculated because height and weight were not obtained.

cardiac areas 5 per cent or more above the predicted value and only four showed cardiac areas 10 per cent or more above. The largest area was 13.3 per cent above the predicted figure.

Transverse diameter was measured in 290 cases* (Fig. 2). In 136 (46.8 per cent) the diameters were 0.5 cm. or more below the predicted values. In 39 (13.4 per cent) the transverse diameters were 0.5 cm. or more above the predicted values. In the latter group 27 cases exceeded the predicted figures by from 0.5 cm. to 0.9 cm. Nine exceeded it by from 1 cm. to 1.3 cm. Three students showed transverse diameters which were 1.6 cm., 2 cm., and 2.2 cm. above the predicted figures. In each of the three, the heart was markedly transverse in position.

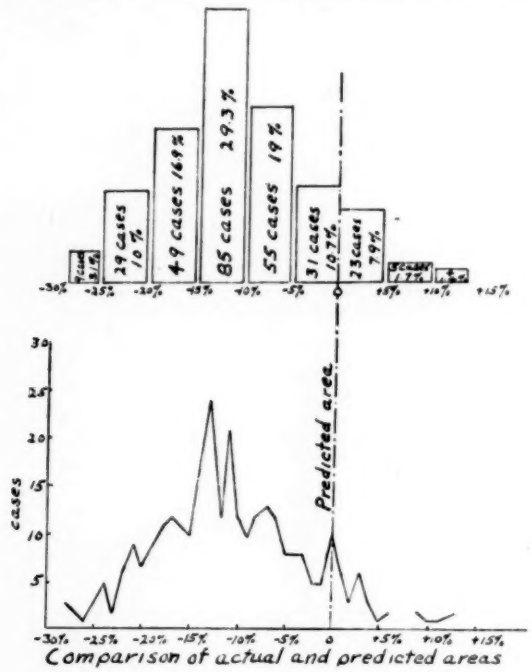

Fig. 1.

Cardiothoracic ratio was determined in 290 cases† (Fig. 3). With the exception of a single student whose ratio was 0.6 the range of variation was 0.37 to 0.53. An examination of the distribution curve shows the vast majority to be in the neighborhood of 0.45. In 247 (85.3 per cent) the cardiothoracic ratios were between 0.40 and 0.50; 24 (8.3 per cent) showed ratios slightly above, and 18 (6.2 per cent), slightly below these figures.

The anteroposterior diameter of the heart was measured in 269 cases, the range of variation being from 45 per cent to 93 per cent of the transverse diameter (Fig. 4). In most cases the anteroposterior diam-

*In one case predicted values were not calculated because height and weight were not obtained.

†In one other case the left margin of chest was not copied.

eter was measured by a line joining the foremost point of the heart with the most posterior point. This line was usually horizontal or slightly diagonal. In some cases, however, in which the angle between

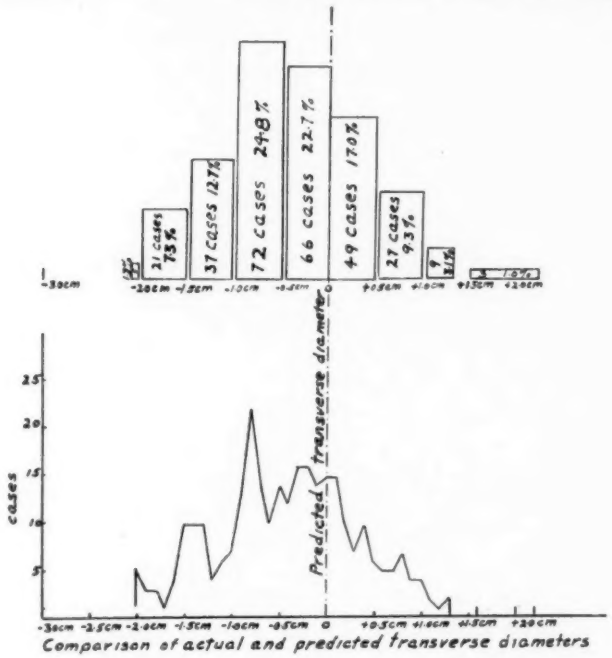

Fig. 2.

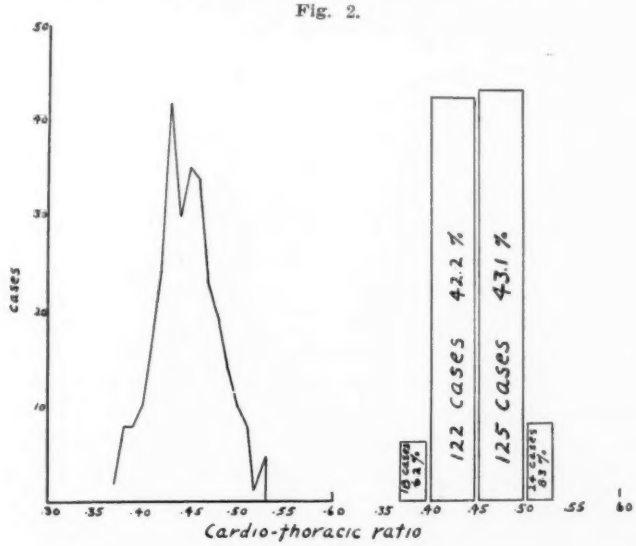

Fig. 3.

this line and the vertical was acute, the anteroposterior diameter was measured in the same manner as the transverse diameter: a vertical line was drawn midway between the spine and sternum and the antero-

posterior diameter considered the sum of the greatest distances which the heart shadow extended in either direction from this line. In 82.6 per cent of the cases, the anteroposterior diameter measured between 60 per cent and 85 per cent of the transverse diameter. These figures are in agreement with those of Roesler,[2] which showed 91.3 per cent of cases with an anteroposterior diameter between 62.5 per cent and 85 per cent of the transverse diameter. His group included both sexes and a wider age group.

DISCUSSION

The two principal roentgenological signs of a cardiac lesion are cardiac enlargement and an abnormal shape of the cardio-aortic shadow. Our studies prompt the following comments upon them:

A. *Concerning Cardiac Enlargement.*—(1) The predicted normal figures of Hodges and Eyster may be too high for young men in this

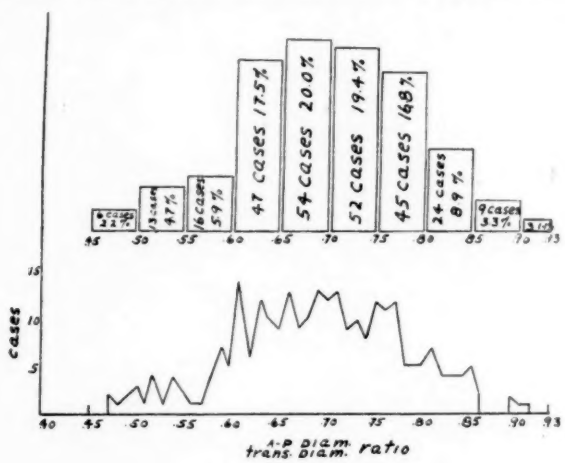

Fig. 4.

age group, and the normal variation allowed on either side may be too narrow. An examination of the distribution curve for cardiac area (Fig. 1) shows that the majority of these subjects fall to the left of the line which marks the predicted value. If this line were moved 10 per cent to the left, it would fall more nearly in the center of the distribution curve. If, in addition, the range of normal variation were considered 15 per cent in either direction, instead of 10 per cent, 272 cases (93.8 per cent) would fall within normal limits, 9 (3.1 per cent) would fall above, and the same number slightly below. Study of the distribution curve for transverse diameter (Fig. 2) shows that the majority of our cases have a transverse diameter which is below the predicted figure. If the line of predicted normal were moved 0.5 cm. to the left and if the normal range on either side were considered to be 1 cm. instead of 0.5 cm., the prediction figures would coincide more nearly with what seems to us correct for our group. (2) In this group

of students when one orthodiagraphic measurement tended to be above normal, its implication was usually neutralized by another measurement. For instance, thirty-eight of thirty-nine cases with a transverse diameter 0.5 cm. or more above the predicted figure, had a cardiothoracic ratio of 0.53 or less. Furthermore, eight of nine subjects with a frontal silhouette area 5 per cent or more above the predicted figure had an anteroposterior diameter which was only from 48 per cent to 71 per cent of the transverse diameter.

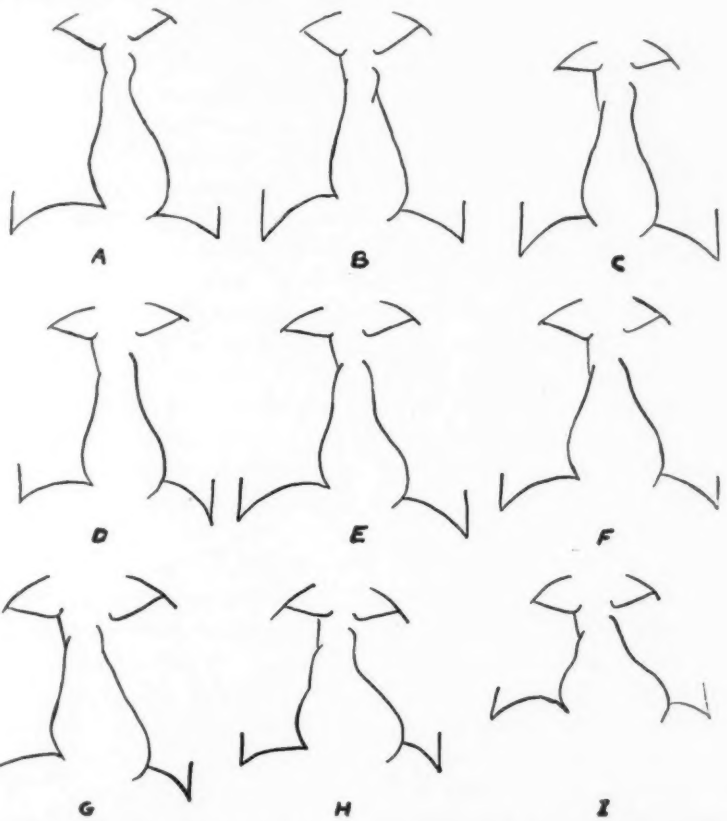

Fig. 5.—Showing the various heart shapes encountered in 291 college students without evidence of cardiovascular disease. The heights and weights of the different individuals are as follows: (*A*) 68 inches, 127 pounds; (*B*) 66½ inches, 130 pounds; (*C*) 66 inches, 122 pounds; (*D*) 70 inches, 138 pounds; (*E*) 69 inches, 148 pounds; (*F*) 70½ inches, 124 pounds; (*G*) 70 inches, 130 pounds; (*H*) 68 inches, 145 pounds; (*I*) 70½ inches, 192 pounds.

B. *Concerning Abnormal Shape of the Cardio-Aortic Shadow.*—Figure 5 shows the various types of silhouettes which were observed. Physique, height of diaphragm, shape of chest, and deformities of the spine influence the shape of the cardio-aortic shadow. Slight degrees of scoliosis are encountered rather frequently. Right scoliosis may produce the so-called mitral configuration. It may also make the aortic knob more readily visible by removing the spine from the background.

Left scoliosis may cause the supra cardiac shadow to appear widened since it displaces the descending aorta to the left. Rotation of the patient to the left in right scoliosis and to the right in left scoliosis tends in most cases to correct the picture and may show the heart to be of normal shape. The descending aorta was visualized in certain of our subjects. Consequently this finding should not be interpreted routinely as indicating arteriosclerosis.

Our observations upon this group of 291 normal students, as well as upon patients with heart disease, make it clear that no rigid roentgenological criteria can be relied upon to determine the presence or absence of heart disease. It is the practice in this clinic to make use of various measurements: the area of the silhouette, the transverse diameter, the cardiothoracic ratio and the anteroposterior diameter. The shape of the heart is also taken into consideration. Any one of these when used alone may be misleading. Together they give a wrong impression less often. In many instances the presence or absence of pathological cardiac enlargement cannot be determined on the basis of x-ray measurements of the heart alone. Furthermore, the diagnosis of heart disease, based upon some abnormality of shape, such as the so-called "mitral configuration," may in certain cases be misleading.

There were thirty-eight cases in which the frontal area of the silhouette was small (20 per cent or more below the predicted figure). In all but four of these, the anteroposterior diameter was of medium length or less (below 85 per cent of the transverse diameter). In this group of cases, therefore, a heart with a small frontal area tended to be small in all its dimensions.

In 1931 we saw two students with unusually large hearts in whom no evidence of heart disease was demonstrated. Both subjects had marked bradycardia. Moreover, many patients with tachycardia and the effort syndrome, without definite signs of heart disease, have been found to have small hearts. These observations have led us to study our present group to see whether it supports the belief that, in a group of normal subjects, unusually small hearts are often associated with tachycardia, and unusually large hearts with bradycardia. The major difficulty is that, for the heart rate, we used the figure obtained from an electrocardiogram taken after the completion of the orthodiagram. The figures are as follows. A. The small heart and tachycardia: Thirty-eight of 291 had small hearts (i.e., the cardiac area was 20 per cent or more below the predicted figure). Of these 38, 4 had a heart rate of over 110, and 2 had a heart rate of between 100 and 110. To approach the question from another direction, 16 of 291 had a heart rate of over 110, and 4 of these had small hearts. Twenty-five of 291 had heart rates of between 100 and 110, and 2 of these had small hearts. Sixteen of 291 had heart rates of 60 or less, and none of these had small hearts. B. The large heart and bradycardia: None of the cases in our group showed really large hearts. The four largest showed

silhouette areas between 10 per cent and 13.3 per cent above the predicted figure. Three of the 4 had heart rates between 60 and 70; the fourth had a rate of 75. Thus, our data seem to suggest some relationship between the extremes of heart size and the extremes of heart rate, but they are not very conclusive.

SUMMARY

1. Orthodiagrams were made in 291 male students between the ages of sixteen and twenty-six years, with no evidence of cardiovascular disease.

2. The measurements suggest that the predicted figures of Eyster and Hodges may be too high for young male adults: that the predicted area is approximately 10 per cent too high, and the predicted transverse diameter 0.5 cm. too long.

3. Hearts which were small in the frontal plane frequently had a small anteroposterior diameter.

4. The shape of the heart varied greatly. It was influenced by (a) physique, (b) height of diaphragm, (c) shape of chest, and (d) spinal deformity. In the vertical or ptotic heart the region of the pulmonary artery was frequently prominent. When combined with a straight left border, it sometimes simulated a "mitral heart."

5. In many cases the shadow of the proximal portion of the descending aorta could be seen above the heart.

6. Measurements of the heart size as well as empirical determinations of cardiac shape should be interpreted with a knowledge of their limitations. In many instances the presence or absence of pathological enlargement of the heart cannot be determined on the basis of x-ray measurements alone.

7. In patients without demonstrable cardiac disease there may be an association between the small heart and tachycardia on one hand, and between the large heart and bradycardia on the other. However, our data do not supply convincing evidence upon this question.

REFERENCES

1. Eyster, J. A. E., and Hodges, F. J.: Estimation of Transverse Cardiac Diameter in Man, Arch. Int. Med. **37**: 707, 1926.
2. Roesler, H.: Relation of Shape of Heart to Shape of Chest, With Special Reference to Antero-Posterior Dimension and Morphology of Various Normal Heart Types: Contribution to Question of Accuracy of Ordinary Roentgenological Methods of Heart Measurement, Am. J. Roentgenol. **32**: 464, 1934.

CARDIAC PSYCHOSIS AND THE SYMPTOM OF ANXIETY*

JOSEPH WORTIS,† M.D.
NEW YORK, N. Y.

IT HAS been known for a long time that patients with heart failure may develop a psychosis from which they recover if the heart failure is relieved. As early as 1806 Napoleon's physician, Corvisart, described the main features of cardiac psychosis: depression, restlessness and irritability, rising in some cases to excitement with confusion, and continuous anxiety. About two years ago we had the opportunity of observing a number of such cases at Bellevue; we shall here describe some of the mental changes that were found and relate them as far as possible to the course and nature of the disease.

A TYPICAL CASE HISTORY

G. M., a sixty-one-year-old man with signs of congestive heart failure, was transferred from a medical ward to the psychiatric service because of unmanageable excitement and delusions. "I heard fellows over there talking of shooting," he said, "and a raid was made the other night. The beds were moved around. The nurse tried to give me some medicine but that man there knocked it down and drank it himself. They got mean with me." "I was very much alarmed," he said next day. "You know the priest came over to see me. . . . I don't know exactly why, but I felt intimidated. I did feel frightened. Whether I should have reason for feeling frightened, I don't remember now. This nurse, instead of handing me the medicine, gave it to some man, and he drank it, and this nurse laughed in the most sneering manner. But I was careful not to make any move, so that they wouldn't think me insane. That man Jack over there—a porter or something—had the most brutal manner, and tried to intimidate me. It looked like an armed protection; there were people there with guns. There was an old man walking up and down in front of me, and he told me, if I wanted to get out, it had better be now. Last night strange things happened, and I don't know whether it was imagination or not, but this man in the bed beside me kept jumping up and looking out of the window. His throat was cut and gashed. . . ."

This patient was talkative and extremely circumstantial during examination, and at times incoherent. He looked very frightened. The persecutory delusions and hallucinations were vividly described, but only vaguely systematized, and had the quality of nightmares. He appeared weak and admitted feeling frightened, but he rested quietly in bed during the examination. The patient at this time was breathless while at rest, orthopneic, and slightly cyanotic. The teleroentgenogram showed an enlarged heart. The first sound at the apex was of poor quality, and the second aortic sound was accentuated. The rhythm was regular; the rate was 88. There were no murmurs. There were moist râles at the bases of both lungs. The liver was enlarged to two fingerbreadths below the costal margin. There was a moderate

*From Bellevue Psychiatric Hospital. Read in part at the joint meeting of the New York Neurological Society and the New York Academy of Medicine, Section of Neurology and Psychiatry, May 12, 1936.

†Research Fellow, Bellevue Hospital, and Research Fellow in Psychiatry, New York University Medical College.

edema of the extremities, and the blood pressure was usually about 180/90. There was moderate sclerosis of the radial arteries. There was also a history of an attack of polyarthritis at the age of seven years, but the physical findings on the whole pointed to hypertension as the cause of the heart disease.

With bed rest and digitalis the patient showed steady improvement within the next week. There were often restlessness at night and paroxysmal dyspnea, sometimes of marked severity, but at the end of two weeks the patient was up and about and was no longer confused. He was fairly lucid in his speech and amiable in manner and no longer had delusions. Though he was still inclined to ramble, he gave the following account of the psychotic episode:

"Everything was like a dream," he said; "I imagined people were against me and were walking about in a sort of gang and acting mean to me. I remember very clearly the incidents that happened—how they stood together in a corner of the ward, and how somebody came over to my bed and drank my medicine. When I came here, I thought people were in the gang against me, too. I remember looking at the nurse and thinking she was a pleasant person—not the kind you would expect to be in a gang, and I thought there must be something wrong. I was suspicious of you and the other doctor. When you asked if I saw things I said no, because I thought it would be used against me. I feel recovered now."

Since the patient showed further physical and mental improvement during the next ten days, he was finally discharged about a month after admission, still somewhat dyspneic, but with no signs of a psychosis.

Three months later the patient returned, again very dyspneic and orthopneic, with pulmonary congestion and an enlarged liver, and again he was psychotic. "I was courteous as I always am," he declared, "but they have been treating me outrageously . . . one of those patients was smoking a pipe, and I could tell it was opium. He lied deliberately about me and had an insulting manner. . . ." The patient was reported to have threatened another patient with a razor. He was again tense and excited, anxious and depressed, but he again responded favorably to treatment and in a month was again discharged, this time to the medical service of Bellevue Hospital. Less than two years later the patient died.

COMMENT

The frequency with which this clinical picture appeared in cases of cardiac psychosis was striking. One could indeed often suspect the presence of heart failure, merely by talking to the patient and watching him. The breathlessness and weakness, the feeble restlessness, the pallor or cyanosis, the tense, pained look and active eyes, the rambling, low pitched, plaintive and often incoherent speech, were all typical. These patients were unable to answer questions to the point; they talked too much and roundabout, complainingly or with an air of indignation. They showed a peculiar responsiveness to distracting details in the surroundings, and it was not easy to hold the patient's attention in examination. The patient might be at once somnolent and hyperacute, lying with half closed eyes, but starting at the least interruption. Many complained of inability to sleep, or of bad dreams or dreamlike hallucinations, they were often not quite sure which. We shall later investigate these symptoms more carefully.

In the course of further observation it appeared that the mental symptoms most frequently seen were confusion, anxiety and persecutory de-

lusions, and often overtalkativeness and circumstantiality. Thus in a small group of five cases they appeared in the order of frequency shown in Table I.

TABLE I

FREQUENCY OF MOST COMMON SYMPTOMS IN FIVE SELECTED CASES OF CARDIAC PSYCHOSIS

NO.	NAME	AGE, SEX	DIAGNOSIS	CONFUSION	ANXIETY	DELUSIONS OF PERSECUTION	OVERTALKATIVENESS	CIRCUMSTANTIALITY
95380	E. P.	49 F.	Arteriosclerotic heart disease, fibroid heart, auricular fibrillation. Class IIb.	+	+	+	+	+
95484	H. O.	50 F.	Arteriosclerotic and hypertensive heart disease, enlarged heart, fibroid heart, regular sinus rhythm. Class IIb.	+	+	+		+
95451	N. R.	39 F.	Rheumatic heart disease, enlarged heart, mitral stenosis and insufficiency, auricular fibrillation. Class III.	+	+	+		
95498	M. S.	37 F.	Rheumatic heart disease, enlarged heart, mitral stenosis and insufficiency, regular sinus rhythm. Class IIb.	+	+	+	+	+
95553	A. H.	60 F.	Arteriosclerotic and hypertensive heart disease, enlarged heart, coronary sclerosis, probable coronary occlusion, regular sinus rhythm and premature ventricular contractions. Class III.	+	+	+	+	+

These clinical impressions were confirmed by observation of another twenty cases, but an effort was made to use more objective methods.

To find out what was typical of the mental picture in cardiac psychosis, it seemed to be necessary to take a large unselected series of cases of heart failure seen on the psychiatric medical service, reduce the material to a relatively uncomplicated series of cases of cardiac failure, and then tabulate the frequency of the leading mental symptoms. A list of one hundred such cases was prepared from the hospital records and the individual case records were then studied.

In this series of one hundred consecutive cases of heart disease in failure it was found that the cases fell into the following groups:

About one-third (thirty-seven subjects) were subjects sixty-five years of age or over with more or less advanced arteriosclerosis, whose mental symptoms could possibly be attributed to senile or arteriosclerotic changes. In the senile group confusion and gross memory defects were

especially prominent. The mental changes, however, were more or less chronic, and the mental picture did not change markedly with the fluctuations in the cardiac reserve. Many of these cases were undoubtedly senile psychoses in which the heart disease was merely a contributing factor.

About one-third (thirty-seven subjects) had other significant complications which could in themselves explain the psychosis. Of these, thirteen were hemiplegic or aphasic, and twelve were alcoholic. Two cases were complicated by pneumonia, while carcinoma and diabetes occurred in each of two other subjects. One patient had an unexplained temperature of 103° F. In four cases there were histories of chronic psychosis; two classified as schizophrenia, one as psychopathic personality, and one as manic-depressive psychosis.* One patient was excluded because the psychosis followed parturition, and in another case the patient died before he was adequately examined. A case of hyperthyroidism was also excluded.

In many of these subjects the psychosis may have been wholly or partly due to the heart failure, but for the purpose of this study it was thought best to eliminate them, so that a final group of only twenty-six subjects remained, all of whom were relatively uncomplicated cases of congestive heart failure. One must say relatively, because there is probably no really uncomplicated case of heart failure. There are for example always the etiologic factors to consider: hypertension, arteriosclerosis, rheumatism, syphilis, and chronic pulmonary emphysema; and these etiological agents are all likely to affect the function of organs other than the heart. Whenever there was no evidence of a central nervous system lesion, however, and no indication of a psychosis preceding the onset of heart failure, and when, moreover, the patient was less than sixty-five years of age and had no other complications likely to produce mental symptoms, the subject was included in this study. In a few of these subjects there was some evidence of kidney damage, subfebrile temperature, or a mild degree of anemia, and in one case there was a cystitis. It may be that these complications contributed to the development of the psychosis, but where they appeared relatively unimportant, the cases were included. It is noteworthy in any case that the age level of the series is so high, but it appeared in the course of the study that the clinical picture of cardiac psychosis in a young individual with uncomplicated rheumatic carditis did not differ in essentials from others in the group.

The findings in the remaining cases are recorded in Table II.

By reference to the table one can see that cardiac psychosis is characterized mainly by confusion, delusions of persecution, and anxiety.

*In two instances the presence of complications was discovered only after the original period of observation, by reference to State Hospital records. One was a case of chronic alcoholism, the other of long-standing manic-depressive episodes. In both cases the original diagnosis of cardiac psychosis was incorrect. Both patients recovered.

TABLE II

TWENTY-SIX CONSECUTIVE CASES OF CARDIAC PSYCHOSIS

NUMBER	NAME	AGE AND SEX	DIAGNOSIS	NO. DAYS OBSERVED	CONFUSED	APPREHENSIVE	DELUSIONS OF PERSECUTION	OVERTALKATIVE	CIRCUMSTANTIAL	OUTCOME
1118*	G. V.	15 M.	Active and inactive rheumatic heart disease, enlarged heart, mitral stenosis and insufficiency, sinus tachycardia. Class IIb.	2	+	+	+	+		Not traced.
169429*	J. J.	55 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart, mitral stenosis and insufficiency, auricular fibrillation. Class III.	11	+				+	Died ten weeks later.
169783*	E. S.	53 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart, auricular fibrillation. Class IIb—III.	15	+	+	+		+	Died three months later.
168835*	J. S.	59 M.	Arteriosclerotic and hypertensive heart disease, coronary sclerosis, enlarged heart. Class III.	10	+	+	+	+		Not traced.
94475*	C. R.	48 F.	Arteriosclerotic, hypertensive and syphilitic heart disease, enlarged heart, dilated aorta. Class IIb.	2	+		+			Died during observation.
94313*	I. H.	63 F.	Arteriosclerotic heart disease, fibrosis myocardii, auricular fibrillation. Class IIb.	12		+	+	+		Not traced.
94297*	M. G.	58 F.	Arteriosclerotic and hypertensive heart disease, enlarged heart, aortic and mitral stenosis. Class IIb.	4	+	+	+	+	+	Not traced.

*Cases marked by an asterisk were personally observed. The data in other cases are from hospital records.

TABLE II—CONT'D

167292*	B. L.	60 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart, coronary sclerosis, fibrosis myocardii, auricular fibrillation. Class IIb.	8	+	+	+	+	+	Died during observation.
94828*	D. R.	41 F.	Active rheumatic heart disease, enlarged heart, mitral stenosis and insufficiency, sinus tachycardia. Class III.	20	+	+	+	+		Died six weeks later.
94906*	W. H.	40 F.	Rheumatic heart disease, enlarged heart, mitral insufficiency and stenosis, auricular fibrillation. Class IIb.	15	+	+	+		+	Died ten weeks later.
93345	M. S.	43 F.	Inactive rheumatic heart disease, enlarged heart, mitral stenosis and insufficiency, auricular fibrillation. Class III.	12	+	+	+	+	+	Died two months later.
93419	S. D.	59 F.	Arteriosclerotic and hypertensive heart disease, enlarged heart, dilated aorta. Class IIb.	10	+		+	+	+	Still psychotic two years later. Hypertensive.
94046	E. J.	44 F.	Syphilitic heart disease, enlarged heart, aortitis, aortic insufficiency, Austin Flint murmur. Class IIb—III.	5	+	+	+	+	+	Died eighteen months later.
168236	D. H.	54 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart, coronary sclerosis. Class III.	40	+	+		+	+	Not traced.
102261	E. V.	36 F.	Rheumatic heart disease, enlarged heart, mitral stenosis, and insufficiency. Class IIb.	17	+	+	+	+		Died ten weeks later.
175797	G. M.	55 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart. Class III.	6	+		+	+		Died during observation.
93135	H. W.	54 F.	Arteriosclerotic and hypertensive heart disease, enlarged heart, dilated aorta, auricular fibrillation. Class III.	25	+		+			Died two months later.
94321	M. W.	59 F.	Arteriosclerotic and hypertensive heart disease, enlarged heart, auricular fibrillation. Class III.	5	+	+	+	+	+	Died one month later.
166755	E. C.	63 M.	Arteriosclerotic heart disease, enlarged heart, coronary sclerosis, fibrosis myocardii, auricular fibrillation. Class III.	15	+		+			Died six weeks later.

TABLE II—CONT'D

NUMBER	NAME	AGE AND SEX	DIAGNOSIS	NO. DAYS OBSERVED	CONFUSED	APPREHENSIVE	DELUSIONS OF PERSECUTION	OVERTALKATIVE	CIRCUMSTANTIAL	OUTCOME
166140	S. F.	56 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart. Class III.	22	+	+	+			Died five weeks later.
95231	S. G.	43 F.	Hypertensive heart disease, enlarged heart, paroxysmal auricular tachycardia. Class IIb.	7	+	+	+			Not traced.
94671	A. W.	50 F.	Syphilitic heart disease, enlarged heart, aortic stenosis and insufficiency, aortitis. Class III.	6	+	+	+	+	+	Died during observation.
93624	C. C.	58 F.	Hypertensive and arteriosclerotic heart disease, enlarged heart, aortic sclerosis and dilatation. Class IIb.	6	+	+	+	+		Not traced.
94136	A. C.	42 F.	Hypertensive heart disease, enlarged heart, sclerosis and dilatation of aorta, aortic insufficiency. Class IIb.	12	+	+		+		Improved. No cardiac failure.
165909	M. B.	62 M.	Arteriosclerotic and hypertensive heart disease, enlarged heart, coronary sclerosis, fibrosis myocardii, auricular fibrillation. Class IIb.	25	+	+	+			Bedridden, seriously ill and psychotic two years later.
			Number		25	20	23	17	12	
			Percentage		94%	77%	89%	65%	46%	
172152*	G. M.	61 M.	Arteriosclerotic and hypertensive (rheumatic?) heart disease, enlarged heart. Class III.	29	+	+	+	+	+	Died eighteen months later.

This tabulation of symptoms, however, has only a qualified significance. Patients who are merely somnolent and comatose are not as often sent to psychiatric hospitals as those who are excited and unmanageable, and the latter are more than likely to show symptoms of anxiety. With due allowance for this qualification, however, the prevalence of anxiety, confusion, and persecutory delusions in these cases is, nevertheless, striking. It will be instructive to compare these results with the findings of other authors.

ON THE HISTORY OF CARDIAC PSYCHOSIS

The early account of Corvisart has already been mentioned. There is a typical case discussed in Corvisart's book. In 1818 Nasse wrote of the prominence of anxiety in cardiac psychosis as of a well-known fact; but even Corvisart and Nasse appear to have had their predecessors. There are references in the writing of Morgagni and of Antonio Guiseppi Testa on the relation of the heart to madness,* but the literature grows less reliable the farther back it goes. Thus Pliny and Valerius Maximus reported the presence of a "cor hirsutium," "hairy heart" or heart with vegetations, in the Messenian Aristomenes, who had alone slain three hundred Lacedaemonians before he died, but this seems to be incompatible with our observations on the cardiac reserve of patients with psychosis.

The literature of the last century was much concerned with the relations between heart and brain, but both the observations and speculations reflect the spirit of an oversimplified materialism, and there was an undue emphasis on the presence of heart murmurs among the insane or of heart lesions at autopsies. The popular association of the heart with the emotions no doubt prepared the way for the promulgation of the theories. One finds, however, descriptions of unmistakable cases of cardiac psychosis in the early literature. Thus Stosch in 1836 gave an excellent description of a typical case, with the heart lesion confirmed by autopsy; the psychosis was marked by confusion, anxiety, and circumstantiality, whereby the patient "spoke continually and with excitement of the most trivial things."

Unfortunately, few authors limited their observations to psychoses associated with actual heart failure. Saucerotte in 1843 on the basis of seven observations (of which at least two were incorrectly diagnosed) was the first to relate definitely the mental changes to "cardiac crisis." Bergmann in 1844 wrote of "metatastic mania proceeding from the heart." Later a considerable number of cases were described. Mildner (1857) appears to have originated the unfounded theory that mitral disease produces depression and aortic disease excitement, and Ziehl in 1854 gave a vivid description of a patient with persecutory delu-

*In the sixteenth century, Amatus Lusitanus wrote on the relation of the heart to madness; later Daniel Sennert, Wepfer, Severinus, Greding, Lieutaud, William Cruikshank, and Soemmering all wrote of the influence of the heart on the brain, or described cardiac lesions in the insane.

sions who had attempted suicide "with an expression of the most awful anxiety on his face." An admirable detailed description of a similar case by Silbernick of Würzburg appeared in 1875. In Italy in 1869 Golgi reported a number of typical cases. In 1882 Lombroso declared that no alienist could any longer doubt the important influence of heart disease in provoking mental disorders. D'Astros (1881) revived Mildner's theory, called attention to the terrifying nocturnal hallucinations and emphasized the grave prognosis. The French literature of this period abounds in typical case histories.

In America in 1884, a Dr. Alice Bennett undertook to discover the incidence of heart disease among the insane and examined five hundred inmates of a women's asylum. She found forty cases of what she considered to be true cardiac psychosis and reported them. "I must ask your forbearance if these prove somewhat monotonous," she wrote, "for it is largely in this very fact that their interest resides." It appeared that the "form of mania with which heart disease was most constantly associated was that characterized in its beginning by hallucinations of hearing with fixed delusions of persecution and a mania of suspicion."

Mickle (1888) in the course of an elaborate study of heart disease associated with insanity cited the case of a porter in his own employ who died of rheumatic heart disease and who had developed a paranoid psychosis as the heart failure progressed.

Benjamin Ball of Paris wrote an excellent short account of cardiac psychosis with case reports in 1890, and descriptions of typical cases are found in papers by Armaingaud (1878), Duplaix (1882), Fauconneau (1890), Eichhorst (1898) and Telgmann (1899). Henry Head as a young house physician (1901) observed the occurrence of the symptom of fear among cardiacs and concluded that "there is no doubt that a state of fear can exist in which there is no fear of any particular object . . . but it is usually so closely mixed up with hallucinations or other manifestations that it becomes peculiarly difficult to investigate."

House (1905) classified the different kinds of mental change associated with heart disease. He emphasized "the state of fear or apprehensions, usually accompanied by more or less panic." "It will be found," he concluded, "that the symptom of fear is commonly found in all the subdivisions and classes." In a valuable study Ducros (1906) came to the same conclusion: cardiac patients are easily frightened and tend to develop delusions of persecution.

In 1909 Alfons Jakob wrote the most comprehensive study of circulatory psychosis that had yet appeared, founded on personal observations, and interpreted with caution and keen insight. Bonhoeffer (1910), the German authority on symptomatic psychoses, did not at first recognize any specific features in cardiac psychosis but later acknowledged the prevalence of anxiety and reported its presence in nine out of twelve cases.

J. I. France (1915) recognized the prevalence of anxiety in cardiac patients, and declared that this "emotional state, arising from a mechanical difficulty, resembles closely that arising from a psychic state, and the emotional state so caused may either remain vague and unexplained, or there may be induced hallucinations and delusions to explain it."

There have been other papers and case reports by Leendertz (1908) and Bolten (1930) in Holland; S. Wasserman of Vienna (1921); Riesman (1921), Hamburger (1923), Viko (1926) and Morris (1931) in America; Arsimoles (1910) and Urechia (1932) in France; and Massini (1924) and Jaquet (1922) in Switzerland; Targowla (1923), Leyser (1924), G. E. Störring (1934), Engel and Mentzinger (1934) in Germany; Castex and Vivaldo (1917) in the Argentine. The clinical pictures are almost invariably the same: confusion and anxiety, with delusions of persecution. Some other studies concerned with pathogenesis need not be mentioned here.

Some recent authors have put considerable emphasis on psychological factors and on the prepsychotic history. The view put forward in this paper is that the delusions of persecution are not essentially psychological in origin, but develop from the organic symptom of anxiety, and that the individual history of the patient is of no fundamental importance in the genesis of the anxiety. We are indebted to Freud for the recognition of this mechanism in the anxiety neuroses. In a remarkable essay written forty years ago he declared that the anxiety neurosis develops from a subjective state of physical tension; "the anxiety neurosis," he said, "has no psychic mechanism, but invariably influences the psychic life, so that anxious expectation, fears, and hypersensitivity to pain are among its many symptoms."* What follows is an application of this theory toward the understanding of cardiac psychosis.

DISCUSSION OF THE SYMPTOMS

Confusion and Anxiety.—The two key symptoms of cardiac psychosis seem to me to be the confusion and the anxiety.

Practically all of the patients showed varying degrees of confusion, especially at night. In the severe cases they appeared to be unable to orient themselves, or even to make accurate perceptions. In the milder cases they were unable to integrate their perceptions into orderly patterns.† The talk of these patients sounded fragmentary and it was very often difficult to grasp connections. The sensory misinterpretations (hal-

*Freud: "Über die Berechtigung von der Neurasthenie einen Symptomencomplex als 'Angstneurose' abzutrennen" (1895). Ges. Schriftem I, p. 306. We shall not here discuss the particular factors to which Freud attributed the state of anxiety in his cases: a state of anxiety can be induced in more than one way.

†According to this description, the confusion does not differ in essentials from what is sometimes called dissociation. I find it difficult to distinguish sharply between the two. Perhaps the underlying organic cause is the same, dissociation being but a milder and more chronic type of confusion. For a valuable discussion of confusion, see Hartmann and Schilder: Zur Klinik und Psychologie der Amentia. Zentr. f. d. g. Neurol u. Psychiat. 35: 356, 1924.

lucinations) and the false integrations (delusions) are thus closely related, and appear to have their common cause in some organic disturbance of the brain itself.

Twenty of twenty-six cases (77 per cent) showed clear evidence of anxiety, but the actual incidence is probably higher, and in none of the cases tabulated as negative could it be said that anxiety was actually absent. Anxiety, especially when associated with confusion, is a less striking symptom than a delusion and was therefore not always noted in the histories. More stoic patients could conceal their fear, even while admitting delusions of persecution, and in other cases the anxiety was inconstant. Some patients were at times in a state of mere anxious expectancy: they were not frightened, but they easily could be. One woman patient, for example, grew very frightened while the syringe was being prepared for a blood specimen and all but fainted when the specimen was taken. Other patients will jump at the sound of a closing door, or start when another patient moves his arm. They are hyperacute, or hyperresponsive, and ordinary sensations or events take on the proportions of a threat to them.* It is this which explains their distractibility. We are obliged to conclude that in cardiac psychosis the patients are not only frightened, but their susceptibility to fright is very much increased.

One may at first attribute the anxiety of the patients to their knowledge that they are seriously ill, or to the presence of hallucinations or delusions, but it is remarkable and significant that many of the most apprehensive patients did not realize that they were ill, and in many cases the anxiety was present while there were no delusions.† "I just feel frightened," a patient will say, "but I don't know why." The appearance and disappearance of the anxiety with the corresponding signs of heart failure indicated that the anxiety in these cases derived from a body state somehow involved in the process of heart failure.

The Delusions of Persecution.—Twenty-three of the twenty-six subjects (89 per cent) had delusions of persecution.‡

Patients with cardiac psychosis usually have hallucinations, especially at night, but these are generally vague and unorganized, and are easily forgotten. Patients often say, "It may have been a dream," and the hallucinations do in fact have dreamlike qualities: shadowy figures outside the window, chloroform under the bed, silver-colored figures on the ceiling, and the like. When imaginary sensations, or misinterpretations,

*Douty (1885) cited the case of a woman in terminal cardiac delirum who mistook the rumbling of a wheelbarrow for a terrible thunderstorm, and the sound of a water tap for the splashing of a huge waterfall.

†The theory that the patient is frightened by his own delusions, as Grandousier was frightened by his monstrous child Gargantua, is seductive, because it seems to blame the fear on some external influence. But to attribute the patient's fright to his frightful delusions is merely to beg the question. We would still have to ask: Why are the delusions frightful?

‡By way of comparison, delusions of persecution have been found to occur in 20 per cent of cases of manic-depressive psychosis, and 56 per cent of cases of schizophrenia, cf. K. M. Bowman and A. H. Raymond: A Statistical Study of Manic-Depressive Psychoses, Am. J. Psychiat. **11**: 111, 1931.

are elaborated into more of a story, we speak of delusions. We must now ask ourselves: In what way does the sensation of anxiety contribute to the content of these delusions?

A simple answer suggests itself: The delusions, if they are to be compatible with the sensation of anxiety, must be threatening; they must, in other words, become delusions of persecution. A patient, for example, would develop a fear amounting to panic when one approached with a syringe for a blood specimen. If the patient happened not to be very confused at the time, he would say, "I feel afraid of the needle." If he was confused, he might mistake the syringe for a gun, and the doctor for a soldier. The result is a delusion of persecution. I think therefore that the delusions of persecution in these cases were a joint product of the anxiety and the confusion.

Anxiety is properly described as fear without a clearly conceived object. In contrast to ordinary fear it has at first no adequate motivation, and the conscious mind attempts to find it one.* One might say that the delusions of persecution were an attempt of the patient to explain his anxiety to himself. That his explanation was so absurd was due in turn to the element of confusion. Many patients were lucid but apprehensive during the day, but definitely confused at night: it was only during the night that these patients had real persecutory delusions. Occasionally a patient shows evidence of anxiety without confusion and without persecutory delusions, but with the relatively reasonable and justifiable fear of dying. If the anxiety were more constant and chronic and the confusion less pronounced, perhaps the setting for a chronic systematized paranoia would be complete. The lack of systematization in cardiac psychosis points to the relative acuteness of the mental changes.

Unmotivated depression is familiar to everybody, but the existence of unmotivated anxiety is less widely recognized. Except that we are dealing with a different mood, the mechanism described here is, however, essentially the same as that found in a depression: as long as the higher levels of consciousness or integration are intact, the patient will provide an apparently reasonable explanation for his mood; when the higher functions are disturbed as well, as they are for example in general paresis, delusions may merge with the depression to produce, let us say, absurd hypochondriacal complaints. One cannot, in other words, think a mood—one can only think a thought, but the nature of the thought will be more or less dependent on the underlying mood. When the underlying mood is anxiety, the specific fear that the patient expresses will proceed from his special predisposition or from his repertoire of

*"'J'ai peur, disait un malade à M. Esquirol.' 'De quoi?' 'Je ne sais rien, mais j'ai peur'." (*Des maladies mentales*, 1838.) Cited by Griesinger.

favorite fears.* G. Stanley Hall has given a full account of the common fears of normal people in his *Study of Fears,* and Burton's *Anatomy of Melancholy* has a long catalogue of paranoid fears and phobias from classical literature. "Pacify them for the one," he wrote, "and they are instantly troubled with some other fear; always afraid of something, which they foolishly imagine or conceive to themselves, which never peradventure was, never can be, never likely will be; troubled in mind upon every small occasion, unquiet, still complaining, grieving, vexing, suspecting, grudging, discontent, and cannot be freed so long as their melancholy continues."†

Other Symptoms.—Seventeen of twenty-six patients (65 per cent) were overtalkative, and twelve out of twenty-six (46 per cent) were circumstantial. The talkativeness may be looked upon as a form of motor restlessness and should not be mistaken for euphoria, and the talk is rambling because the patient is confused. The patient dwells on details because they have become unduly important to him. It may be that the talk is importunate and querulous because the patient feels he needs to explain and justify himself to an unsympathetic observer. Not all patients are talkative, however, and some of the patients are so suspicious that they become unduly reticent.

Sometimes there is a bitter and aggressive reaction to the sensation of distress. The persecutory ideas are diffuse and correspond to the formula: "The whole world is against me."

Since the anxiety is often marked, the patient's delusions involve threats of bodily harm; the patient may attempt suicide or attack his supposed persecutors. It is often some such act that brings the patient to the psychiatric hospital.

Patients often complain of imaginary odors, "smoke in the room," "ether" or "chloroform," or simply "heavy air." A particularly common kind of dreamlike delusion is that of being covered with a cloth, or wet rag, or being "hit over the face with a towel." It may be that all such delusions are referable to the respiratory distress. Delusions of being moved about or rhythmically up and down may be vestibular in origin.‡ Rhythmic auditory hallucinations with repetition of a single word or syllable are also described by some patients. Death and murder are frequent subjects of delusions, though the patient may project the death or murder to another person. "There was a woman in the bed beside me dying of heart disease," one woman patient said, "and the doctors came and took her insides out, but next morning she was alive again." The theme of death and resurrection reappeared several times in different subjects.

*Roubinovitch (1895) was able to show that the delusional phobia which found expression during a cardiac psychosis was already present to a mild degree before the onset of heart failure.

†Part. 1, Sect. III, Mem. I, Subs. II.

‡Cf. Schilder, Paul: The Vestibular Apparatus in Neurosis and Psychosis, J. Nerv. and Ment. Dis. 78: 1, 1933.

The psychological mechanisms here brought into play furnish interesting material for further study, but it suffices here to say that the content of the psychosis is modified on the one hand by the nature of the physical disease and on the other by the past experience of the patients. In other words, the psychosis, like a dream, reveals the patient and his complexes. The patient can talk and think only in terms of these experiences and complexes, for they are the only language he knows. But the *content* of the psychosis does not explain its *cause*, any more than the content of a dream explains the cause of dreaming.

THE DIAGNOSIS OF CARDIAC PSYCHOSIS

Some authors believe that only 1 per cent of patients with cardiac disease develop a psychosis. Lilienstein declares that fully 90 per cent of patients show some degree of mental change. A. G. Gibson found that 10 per cent of his cases showed major mental symptoms. Wyckoff* estimated that 8 per cent of the cases on his medical service at Bellevue showed mental symptoms.† Even when mental changes occur, an anxiety psychosis is by no means the rule, or even common, in advanced heart failure. Mild depression and somnolence may be more frequent, but they hardly require the special care of a psychiatric hospital. On the other hand, the occurrence in any particular case of the same clinical picture does not prove the presence of a cardiac psychosis. The present study gives no information on the specificity of the clinical picture described here since no other groups of organic psychoses were studied for comparison. It is not difficult, however, to find cases with a clinical picture differing in no essentials from those here described, perhaps even associated with dyspnea, but with no history or findings suggesting heart disease. My own impression is that the same clinical picture may occur elsewhere, but much less frequently and typically, and at any rate it is known that shock, hemorrhage, head injury, brain tumor, and a variety of drugs may all produce a combination of confusion and anxiety associated with persecutory delusions. A similar syndrome is produced by spontaneous hypoglycemia, and is relieved by a piece of candy. Wolff and Curran found that anxiety and persecutory delusions are almost a regular occurrence in a variety of symptomatic psychoses associated with conditions ranging from alcoholism and copper poisoning to carbuncle and malaria. Though it is probable that each of these agents tends to produce different mental pictures, there is always some overlapping and there are always some common features; but even the occasional occurrence of the same clinical picture in other diseases indicates that "cardiac" psychosis is due to something physi-

*Lecture notes for Bellevue medical students.

†Horner (1910) found that valve lesions were revealed at autopsy in a high proportion (21 per cent) of fatal cases of acute "dementia praecox." It is probable that many of these cases were cardiac psychoses.

ologically more fundamental than circulatory failure—perhaps anoxemia* or some other nutritional deficiency in the nerve cells—which may occur in a variety of diseases.

But even when the psychosis is associated with cardiac symptoms, there are several considerations that must be remembered in diagnosing cardiac psychosis. The first is that the heart disease and failure must themselves have some cause, and this etiologic factor may quite independently cause a psychosis. Syphilitic heart disease, for example, may be associated with general paresis, or arteriosclerotic heart disease with senile dementia. Similarly, the same acute infection which leads to myocardial damage and heart failure may independently cause a psychosis.

The second consideration is that sensations around the heart, especially cardiac pain, are peculiarly common in all kinds of psychoses. On the one hand, strong emotions react upon the heart, and on the other hand, both heart and brain are peculiarly sensitive to common noxae.† In diabetic ketosis and in hypoglycemic shock, for example, the patient will experience anxiety and complain of pain around the heart; while low oxygen pressure, to give another example, may produce both confusion and precordial pain.‡

Finally, cardiac or precordial sensations of various origin, even, says Wenckebach, an intercostal neuralgia, are especially likely to produce anxiety, whether as a specific visceral sensation or simply as a conditioned association, one cannot yet say. Stransky (1903) appears to be the first to have related the symptom of psychotic anxiety to an imaginary visceral sensation from the heart. Braun has written two stimulating but unconvincing books to support the claim that all anxiety comes from or through the heart. "All anxiety," to quote Fleming, "is a mild angina pectoris." But the transitory sensations produced by tachycardia, premature ventricular contraction, or an anginal attack are not usually associated with confusion and do not produce a psychosis.

The main criteria in diagnosis are the association of the psychosis with an episode of heart failure, the presence of a typical clinical picture, and the absence of complicating features.

---

*See Hitzenberger, Karl: Über Störungen des Bewusstseins bei Kreislaufkranken infolge Sauerstoffmangels, Wien. Klin. Wchnschr. **46**: No. 28, 1933. Anxiety can be described in physiological terms as a state of hyperexcitability and hyperresponsiveness of the nervous apparatus. Anoxemia has been experimentally shown to induce such a state, cf., eg.: N. Morris: Anoxemia and the Increased Electrical Excitability of the Neuro-myone, Brit. J. Exper. Path. **3**: 101, 1922; also Heinbecker and Bishop: Effect of Anoxemia, CO_2, and Lactic Acid on Electrical Phenomena of Myelinated and Unmyelinated Fibres of the Autonomic Nervous System, Am. J. Physiol. **96**: 613, 1931.

†Cannon, W. B.: Stresses and Strains of Homeostasis, Am. J. Med. Sc. **189**: No. 1, 1935.

‡Cf. Rothschild and Kissin: Production of Anginal Syndrome by Induced General Anoxemia, AM. HEART J. **8**: 729, 1933: also McFarland, Ross A.: The Psychological Effects of Oxygen Deprivation (Anoxemia) on Human Behavior, Arch. of Psychology, No. 145, Dec., 1932.

COURSE AND PROGNOSIS

After the tabulation of our series of cases, it was noticed that practically all of the subjects had advanced heart failure and fell into the functional class specifications IIb and III of the American Heart Association. Subjects with only slightly diminished cardiac reserve almost never developed a psychosis. All of the patients had a degree of dyspnea sufficient to interfere seriously with ordinary activity, though not all of the patients showed dyspnea while at rest. One is entitled to conclude tentatively at least that the development of the psychosis is ordinarily associated with a considerable degree of dyspnea. Apparent exceptions to this rule proved to be cases of cerebral embolism, thrombosis, hemorrhage, or senile psychoses associated with heart disease. Practically all of the cases in the series developed the psychosis only after the heart failure had persisted for some time; in none of the cases did the psychosis precede the onset of failure. In most of the cases the psychosis survived the period of extreme or congestive failure by a few days or even weeks.*

No cases were observed in which the psychosis was static, or survived as a chronic psychosis after the cardiac failure was relieved.

Of the twenty-six patients listed in our table, seven could not be traced. Of the remaining nineteen, sixteen had died within the following two years, and three were still alive. Of these, two were in State Hospitals, one bedridden and seriously ill, the other up and about but still psychotic and with severe hypertension. A single patient was attending the cardiac clinic and was said to be improved. Of the sixteen known deaths, four had occurred within the period of observation and eight within three months after the period of observation.

The high mortality rate of this series indicates that the psychosis is a bad omen. It indicates a failure of the central nervous system, following upon and complicating the failure of the circulation. The elaborate physiological mechanism called into play to compensate for the deficiency of circulation has broken down, and the course thereafter is downhill.

SUMMARY AND CONCLUSIONS

We could not estimate the frequency of psychosis in heart failure (but it is generally admitted to be uncommon); nor did we try to explain the fundamental cause of the psychosis, which is still unknown. We have simply investigated some clinical features of the psychosis when it occurs. It was found to be mainly characterized by confusion, anxiety, and delusions of persecution, and the patients were often overtalkative

*This discrepancy between the period of psychosis and the period of extreme failure led to the erroneous belief that the psychosis was due to the resorption of the poisonous disintegration products of edema, rather than to the circulatory failure as such. This theory was advanced by Eichhorst forty years ago. There is, however, no relation between the absorption of the edema, as measured by loss of weight and increased diuresis, and the onset or duration of the psychosis.

and circumstantial. The development of a psychosis in the course of heart failure appears to be of grave prognostic significance, for of nineteen patients who could be traced, sixteen had died during, or within two years after, the period of observation.

In addition, the study of the psychosis led to several other conclusions: (1) that anxiety is a body state and can be provoked by physical disease, (2) that anxiety may induce delusions of persecution, and (3) the persecutory delusions are dependent on the degree of associated confusion. Cardiac psychosis thus directs attention to a fundamental psychological mechanism and furnishes at the same time a well-circumscribed condition in which the physical or physiological basis of anxiety can be studied.

This study was completed during the tenure of a research fellowship and was made possible by the kind cooperation of the Medical Department of Bellevue Psychiatric Hospital under Dr. Norman Jolliffe.

REFERENCES

Ameghino, A.: Existe una locura cardiaca? Rev. Asoc. méd. argent., Buenos Aires, Soc. de neurol. y psiquiat. **37**: 163, 1924.

Armaingaud: Sur une relation pathogénique entres les maladies du coeur et l'hystérie chez l'homme. Mém. et bull. de la Soc. de méd. et de chir. de Bordeaux, 1878.

Arsimoles, L.: Troubles mentaux dans les maladies du coeur, Écho méd. du nord. **14**: 189, 1910.

Auban and Beurnier: Délire de type maniaque chez un cardiaque, Toulouse méd., 2.s. **2**: 216, 1909.

Arndt, R.: Über die haüfig zu beobachtende Verstärkung des Aortentones bei Geisteskranken, Deutsche med. Wchnschr. **8**: 359, 1881.

Bagot, M.: Des complications cérébrales des affections cardiaques, Thèse de Paris, 1881.

Ball, B.: De la folie cardiaque, Médecine moderne **1**: 557, 1890.

Benda, T.: Über den Zusammenhang von Herz und Geisteskrankheiten, Berlin, 1881.

Bennett, Alice: Relation of Heart Disease to Insanity, Tr. M. Soc. Pennsylvania **16**: 103, 1884.

Bergmann: Mania metastatica von Herzen ausgehend, Allg. Zeit. f. Psychiat. **1**: 574, 1844.

Bignon, J.: Des accidents cérébraux et en particulier des accidents psychiques dans les maladies chroniques du coeur, Paris, 1880.

Bolten, G. C.: Psychosen ten gevolge von Hartandoeningen, Geneesk. gids. **8**: 362, 1930.

Bonhoeffer, K.: Die symptomatischen Psychosen, Leipzig and Vienna, 1910, F. Deuticke.

Braun, Ludwig: Herz und Psyche, Leipzig and Vienna, 1920, F. Deuticke.

Braun, Ludwig: Herz und Angst, Vienna, 1932, F. Deuticke.

Burman, J. W.: Heart Disease and Insanity, West Riding Lunatic Asylum Reports **3**: 216, 1873.

Castex, M. R., and Vivaldo, J. C.: Los trastornos mentales en los cardiacos, Prensa med. argent. **3**: 317, 1916-17.

Coombs, C. F.: Mental Disorder in Cardiac Disease, J. Ment. Sc. **74**: 250, 1928.

Corvisart, Jean-Nicolas: Essai sur les maladies et les lésions organiques du coeur, Paris, 1806, Migneret.

Curtin, R. G.: The Delirium Noticed in Cardiac Disease, Philadelphia Hosp. Rep. **6**: 10, 1905.

D'Astros, L.: Étude sur l'état mental et les troubles psychiques des cardiaques, Thèse de Paris, 1881.

Douty, J. Harrington: The Mental Symptoms of Aortic Regurgitation: With a Summary of the Notes on Fourteen Cases, Lancet **2**: 336, 1885.

Ducros, Marcel: Recherches sur la valeur des troubles psychiques dans maladies du coeur, Paris Thèses, 1906-07, No. 17.

Duplaix: Troubles psychiques, hallucinations dans un cas d'insuffisance tricuspide, Encéphale **2**: 287, 1882.

Eichhorst, N.: Toxämische Delirien bei Herzkranken, Deutsche med. Wchnschr. **24**: 389, 1898.

Engel, R., and Mentzingen, A. von: Psychotische Zustandsbilder und cerebrale Herdsymptome bei dekompensierten Herzkranken, Deutsches Arch. f. klin. Med. **176**: 163, 1933-34.

Fabre, Augustin: La folie dans les affections cardiaques, from "Les relations pathogéniques des troubles nerveux," Paris, 1880, V. A. Delahaye.

Fauconneau, J.: De la folie d'origin cardiaque ou des troubles psychiques consecutifs aux maladies du coeur, Thèse de Paris, 1890.

Felberbaum, D., and Finesilver, B.: Cerebral Manifestations of Heart Disease, M. J. & Rec. **129**: 247, 1929.

Fiessinger, C.: La psychologie du cardiaque, Rev. de l'hypnot. et psychol. physiol. **17**: 303, 1902-03.

France, J. I.: Some Observations on the Nervous and Mental Symptoms of Heart Disease, J. A. M. A. **64**: 652, 1915.

Gibson, A. G.: Mental Changes in Heart Disease, J. Ment. Sc. **76**: 632, 1930.

Hamburger, W. W.: Acute Cardiac Psychoses: Analysis of the Toxic and Circulatory Factors in Five Cases of Acute Confusion, Med. Clin. North America **7**: 465, 1923.

Head, Henry: Certain Mental Changes That Accompany Visceral Disease, Brain **24**: 345, 1901.

Herz, M.: Die Angst der Herzkranken, Prag. med. Wchnschr. **25**: 271, 1910.

Hirtz, Lucien: De quelques manifestations cérébrales dans les affections cardiaques, Thèse de Paris, 1877.

Horner, A. A., Jr.: Incidence of Heart Disease in Acute Psychoses, Boston M. & S. J. **163**: 200, 1910.

House, W.: The Psychoses of Heart Disease, J. A. M. A. **45**: 1306, 1905.

Jakob, A.: Zur Symptomatologie, Pathogenese und pathologischen Anatomie der "Kreislaufpsychosen," J. f. Psychol. u. Neurol. **14**: 209; and **15**: 99, 1909.

Jaquet, A.: Über nervöse und psychische Störungen bei Herzkranken, Schweiz. med. Wchnschr. **52**: 245, 1922.

Kiernan, J. C.: Insanity and Cardiac Disease, Am. J. Neurol. & Psychiat. **3**: 32, 1884.

Klingmann, T., and Millett, M. S.: Significance of Circulatory Disturbance in Certain Psychoses After Fourth Decade of Life, J. Michigan M. Soc. **31**: 694, 1932.

Krisch, Hans: Die Symptomatischen Psychosen und ihre Differentialdiagnose, Berlin, 1920, Karger.

Leendertz, P. P.: Intoxicatie psychose bij hartlijden, Psychiat. en Neurol. Bl. Amst. **12**: 530, 1908.

Leyser, E. P.: Herzkrankheiten und Psychosen; eine klinische Studie, Abhand. a. d. Neurol. (etc.), Berlin, 1924, Heft 25, 7.

Lilienstein: Psychoneurosen bei Herzkrankheiten, Arch. f. Psychiat. **52**: 954, 1913.

Limbo: Contribution à l'étude des encéphalopathies d'origine cardiaque, Thèse de Paris, 1878.

Lombroso, C., and Ferri, E.: Su A. Faella e sugli osteomi e le cardiopatie negli alienati, Arch. di psichiat. etc. **3**: 118, 1882.

Malherbe, A.: Folie; insuffisance aortique; hypertrophie du coeur; mort subite, Franç. méd. **14**: 301, 1867.

Massini, R.: Über Delirien bei Herzkranken, Schweiz. med. Wchnschr. **54**: 397, 1924.

Matsuoka, R.: Über die psychischen Störungen bei den Herzkrankheiten, Mitt. a. d. med. Akad. zu Kioto **11**: 308, 1934.

Mickle, W. J.: Goulstonian Lectures for 1888: On Insanity in Its Relation to Cardiac and Aortic Disease and Phthisis, Brit. M. J. **1**: 503 and 575, 1888.

Mickle, W. J.: Aortic Aneurysms and Insanity, Brain **12**: 117, 1889.

Mildner, Emanuel: Aus d. kk. Irrenanstalt in Wien, Beitr. z. Monatsr. f. d. Monat April, Wien. med. Wchnschr., Nos. 46 and 48, 1857.

Moersch, F. P.: Nervous and Mental Phenomena Associated With Paroxysmal Tachycardia, Brain **53**: 244, 1930.

Morris, N.: Mental Concomitants of Heart Disease, U. S. Vet. Bur. Med. Bull. **7**: 651, 1931.

Mouisset, F., and Gaté, J.: Troubles psychiques, hystéro-épileptiques chez une cardiaque, Rev. de méd. **32**: 428, 1912.

Muller, L. R.: Über die Beziehungen von seelischen Empfindungen zu Herzstörungen, München. med. Wchnschr. **53**: 14, 1906.

Murrati, E.: Des troubles mentaux dans l'asytolie, Thèse de Paris, 1880.

Mut, Antonio: La Angustia cardiaca y su Tratamiento, Revista iberoamer. de ciencias médicas. **9**: 60, 1934.

Nasse, Friedrich: Von der psychischen Beziehung des Herzens, Ztschr. f. psychische Aerzte **1**: 49, 1818.

Parant, Victor: La folie chez les cardiaques, Ann. méd.-psychol. 7s. **9**: 419, 1889.

Pelnar, J.: Troubles psychiques au cours des maladies du coeur, Cong. intern. de med. C., 1903. Madrid, sect. de path. int. **14**: 586, 1904.

Riesman, D.: Acute Psychoses Arising During the Course of Heart Disease, Am. J. M. Sc. **161**: 157, 1921.

Roubinovitch: À propos des phobies dans un cas d'insuffisance mitrale. Ann. méd.-psychol. 8s. **2**: 106, 1895.

Roulland, A.: Des folies dites cardiaques, Poitou méd. **4**: 145, 1890.

Saathoff, L.: Herzkrankheit und Psychose, München. med. Wchnschr. **57**: 509, 1919.

Satterthwaite, T. E.: Psychopathies and Neuropathies of Cardiovascular Diseases, New York M. J. **111**: 617, 1920.

Saucerotte: De l'influence des maladies du coeur sur les facultés intellectuelles et morales de l'homme, Ann. méd.-psychol. **4**: 173, 1843.

Silbernick, Kadisch: Ueber Delirien bei Herzkranken, Würzburg, 1875.

Störring, G. E.: Zur Psychopathologie und Klinik der Angstzustände, Berlin, 1934, S. Karger.

Stosch: Manie in Folge eines organischen Herzleidens, Wchnschr. f. d. ges. Heilk., Berl., p. 481, 1836.

Stransky, E.: Zur Klinik und Pathogenese gewisser Angstpsychosen, Monatschr. f. Psychiat. u. Neurol. **14**: 128, 1903.

Strooman, G.: Über die psychotischen Störungen bei dekompensierten Herzkrankheiten, speziell über die Zusammenhänge mit der therapeutischen Entwasserung, Nervenarzt **3**: 396, 1930.

Targowla, R.: Folie cardiaque et insuffisance ventriculaire gauche, Bull. et mém. Soc. méd. d. hôp. de Paris 3s. **47**: 615, 1923.

Telgmann, J.: Toxämische Delirien bei Herzkranken, Deutsch. med. Wchnschr. **25**: 305, 1899.

Theisen, A. C.: Über psychische Störungen bei Herzkranken, Kiel, 1916.

Urechia, C. I.: À propos de la psychose cardiaque, Arch. internat. de neurol. **51**: 473, 1932.

Van Lier, J. L.: Mental Disease and Heart, Nederl. tijdsch. v. geneesk. **2**: 2661, 1925 (Abst. J. A. M. A. **86**: 660, 1926).

Viko, L. E.: Cardiac Neurosis Associated With Rheumatic Valvular Heart Disease, Am. Heart J. **1**: 539, 1926.

Vorobyeff, V.: O nervenïkh razstroĭstvakh pri serdechnïkh bolïenznyakh. (Nervous Disturbances in Cardiac Diseases.) French abstract in Cong. internat. de med., 1897, Moscow, III. sect. **5**: 295, 1899.

Wasserman, S.: Zur Entstehungsweise der Kreislaufpsychosen. Wien. Arch. f. inn. Med. **18**: 449, 1929.

Wasserman, S.: Über psychische Störungen in Verbindung mit dem Cheyne-Stokeschen Psychose, Med. Klin. **17**: 814, 1921.

Weber, A. N.: Über psychische Störungen bei Herzkranken, Jena, 1901.

Weiss, S.: Interaction Between Emotional States and Cardiovascular System in Health and in Disease, Libmann Anniv. Vol. **3**: 1181, 1932.

Wenckebach, K. F.: Herzkranke, die es nicht sind, Wien. med. Wchnschr. **84**: 621, 650, 1934.

Witkowski, L.: Über Herzleiden bei Geisteskranken, Allg. Ztschr. f. Psychiat. **32**: 347, 1875.

Wolff, N. G., and Curran, D.: Nature of Delirium and Allied States, Arch. of Neurol. and Psychiat. **33**: 1175, 1935.

THE MECHANISM OF IMPAIRED AURICULOVENTRICULAR CONDUCTION IN ACUTE RHEUMATIC FEVER*

HOWARD G. BRUENN, M.D.
NEW YORK, N. Y.

IMPAIRMENT of auriculoventricular conduction is common during the course of acute rheumatic fever. Its importance is accentuated by the present-day concept that it indicates active rheumatic carditis.[1] According to various authors,[1-4] the incidence of conduction defects in this disease varies from approximately 27 to 87 per cent in the different series reported. This wide range is probably due, in part, to the varying frequency with which electrocardiograms are taken and, in part, to the severity of the cases studied. According to figures given in the literature, approximately from 28 to 30 per cent of all cases of acute rheumatic fever observed in a general medical service show some degree of heart-block during the course of the disease.

Three theories have been advanced in explanation of this disturbance. The first, or anatomical, is the most commonly accepted. It implies the presence of structural changes involving the auricles and the bundle of His, in the form of acute inflammation, vascular changes, edema, and fibrosis. The second theory ascribes the abnormality to a direct effect of toxins on the conduction system. According to a third hypothesis, there is a heightened vagal action or an increased response to vagal control under the influence of the toxins of the infection.

In studying serial electrocardiograms in a case of acute rheumatic fever with impairment of auriculoventricular conduction, the transient character of the block is impressive. It usually makes its appearance at the height of the activity of the disease. In most cases, the conduction defect will subside within a few days or several weeks; in the majority of cases it tends eventually to return to within normal limits. It is the purpose of the study reported in this paper to attempt to analyze the mechanism of this disturbance.

The study is based on twenty-two patients with acute rheumatic fever who were admitted to the wards of the Medical Service of the Presbyterian Hospital during the last three years. There were nine males and thirteen females. The average age was 25.3 years, with a range of from 9 to 42 years. In every case, the diagnosis of acute rheumatic fever was

*From the Department of Medicine, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital.

This investigation was aided by a grant from the Josiah Macy, Jr., Foundation.

A preliminary report of this work has already been published. See Bruenn, H.G.: Effect of Atropine on Impaired Auriculoventricular Conduction in Rheumatic Fever, Proc. Soc. Exper. Biol. & Med. 32: 562, 1934.

made on ample clinical and laboratory evidence, i.e., polyarthritis, which subsided rapidly with salicylate therapy; high sedimentation rate; leucocytosis; and fever. Twenty of the patients showed evidence of cardiac damage by the presence of valvular defects. Congestive heart failure was not present in any. Each case showed impairment of auriculoventricular conduction in the electrocardiogram. The degree of block varied from prolongation of the P-R interval above 0.2 sec. to incomplete heart-block. None of the patients had received digitalis or quinidine. Salicylates were being administered to over half of the cases at the time of the experiments. In several cases observations were made before and after salicylate therapy.

The behavior of the conduction times in these patients, and in a control group of seven individuals of comparable age without evidence of heart disease, and presenting normal electrocardiograms, was studied after the intravenous injection of atropine or the subcutaneous injection of epinephrine. Two control electrocardiograms were taken, one hour apart. Further records were then made at intervals of from one to four minutes during the periods of observation.

Atropine.—It has been shown that relatively large amounts of atropine must be administered in order to produce paralysis of the terminals of the vagus nerves in the heart.[5] Enough of the drug was given to these patients to produce dryness of the mouth in all cases; pupillary dilatation and flushing of the skin occurred occasionally, but no undue subjective discomfort was induced. It was found that from 1.5 to 3 mg. of atropine sulphate injected intravenously sufficed to produce these symptoms. The maximum effect of the drug occurred during the first fifteen minutes after the injection. In a number of cases, observations were continued over a period of six hours; at the end of this time the ventricular rate and the auriculoventricular conduction time had returned approximately to their control levels. In every case the action of the drug had disappeared completely in the course of twenty-four hours. A series of thirty observations was made on the group of twenty-two rheumatic subjects.

The intravenous administration of atropine sulphate to individuals without evidence of heart disease is characterized by an acceleration of the ventricular rate within the first minute after injection. This acceleration, in the control group, was found to be 42 beats per minute on the average. The range was from 20 to 57 beats per minute. The conduction time before atropinization varied from 0.13 to 0.17 sec., with an average of 0.147 sec. Following the administration of the drug, the average decrease in conduction time was found to be 0.014 sec., with a range of 0.01 to 0.03 sec. (Table I).

In 20 of the 22 patients comprising the rheumatic group (91 per cent), shortening of the conduction time exceeding the limits set by the

TABLE I

EFFECT OF INTRAVENOUS INJECTION OF ATROPINE SULPHATE UPON VENTRICULAR RATE AND AURICULOVENTRICULAR CONDUCTION TIME IN PATIENTS WITHOUT HEART DISEASE*

CASE	AGE	SEX	CONTROL		AFTER ATROPINE INJECTION				CHANGE AFTER ATROPINE	
			VENTRICULAR RATE	P-R INTERVAL (SEC.)	AMOUNT GIVEN (MG.)	TIME OF MAXIMUM CHANGE (MIN.)	VENTRICULAR RATE	P-R INTERVAL (SEC.)	VENTRICULAR RATE	P-R INTERVAL (SEC.)
1	23	F	65	0.15	2.0	10	122	0.14	57	0.01
2	13	M	90	0.13	1.5	5	140	0.12	50	0.01
3	36	M	75	0.17	2.0	10	100	0.16	25	0.01
4	35	M	110	0.13	1.8	1	150	0.11	40	0.02
5	13	M	105	0.13	1.5	6	140	0.12	35	0.01
6	25	M	75	0.17	2.0	10	100	0.16	25	0.01
7	35	M	112	0.14	1.8	5	145	0.11	33	0.03
Average	24.3		90.3	0.147					38	0.014

*None of these patients received aspirin.

control group was noted after atropinization. The decrease in auriculo-ventricular conduction varied from 0.04 to 0.17 sec., with an average of 0.07 sec. A typical protocol is given in Table II.

TABLE II

EFFECT OF EXERCISE AND INTRAVENOUS INJECTION OF ATROPINE SULPHATE IN A PATIENT WITH ACUTE RHEUMATIC FEVER

A. S., Female, Aged 25 years. Mitral Stenosis and Insufficiency. U. H. 450891

DATE 1935		TIME	VENTRICULAR RATE	P-R INTERVAL (SEC.)	REMARKS
April 27		10:30	90	0.22	
April 29		11:10	90	0.24-0.25	
May 2		10:25	80	0.24	
May 3	*Control*	9:20	90	0.23	
	Control	10:14	102	0.23	Exercise*
		10:16	105	0.21-0.23	
		10:17	90	0.24	
		10:19	90	0.24	
		10:21	95	0.23	
		10:26	86	0.24	
		10:31	85	0.24	
		10:46	88	0.25	
		11:16	90	0.24	
		11:43			Atropine 1.5 mg.
		11:44	105	0.18	
		11:46	110	0.18	
		11:48	115	0.18	
		11:53	110	0.17	
		11:55			Mouth dry, face flushed
		11:58	110	0.18	
		12:13	110	0.20	
		12:43	105	0.22	
		1:43	85	0.23	
		2:43	80	0.24	
		3:43	65	0.25	
		4:43	58	0.25	
May 4		10:20	90	0.24	
May 13		2:25	70	0.22	
May 20		10:25	70	0.20	

*Exercise consisted of sitting up and lying back in bed fifty times within two minutes.

In general, it was found that the greater the degree of block before giving atropine, the greater the decrease of the P-R interval following injection of the drug.

The change in ventricular rate ranged from –5 to +65 beats per minute, with an average acceleration of 26.4 beats per minute. There was no uniformly consistent relationship between the degree of acceleration of rate and the extent of shortening of the conduction time. In one case an increase of 50 beats per minute was accompanied by a decrease of only 0.04 sec. in conduction time. In another instance there was a decrease of 5 beats in ventricular rate following injection of atropine, associated with a decrease of 0.17 sec. in the P-R interval. The latter case is illustrated (Table III) in order to show the complete independence of these two factors from each other under the given experimental conditions.

TABLE III

INTRAVENOUS INJECTION OF ATROPINE SULPHATE IN A PATIENT WITH ACUTE RHEUMATIC FEVER. MARKED DECREASE IN AURICULOVENTRICULAR CONDUCTION TIME WITH SLOWING OF VENTRICULAR RATE

G. W., Female, Aged 23 Years. Mitral Stenosis and Insufficiency. U. H. 354940

DATE 1936		TIME	VENTRICULAR RATE	P-R INTERVAL (SEC.)	REMARKS
May 19	*Control*	10:59	88	0.33	
	Control	2:17	105	0.33	
		2:18			Atropine 2 mg.
		2:19	100	0.16	
		2:22	102	0.16	
		2:24	106	0.16	
		2:29	110	0.16	Mouth dry
		2:34	100	0.17	
		2:45			Mouth dry
		2:49	103	*	
		3:19	95	0.29	
		4:19	76	0.33	
May 20		9:55	95	0.17-0.37	
May 21		11:20	75	0.33	
May 22		10:00	90	0.29	
May 28		2:40	70	0.16	
June 1		11:23	75	0.15	

*Prolonged conduction; P-waves superimposed on the T-waves.

In two patients the degree of block was unaffected by atropine. One died suddenly in another hospital six weeks after our observations were made. The other has been followed for almost a year, during which the auriculoventricular conduction time has been persistently prolonged, probably due to fibrosis of the junctional tissues resulting from rheumatic lesions. In nineteen of the cases in which atropine was effective in reducing the degree of block, normal auriculoventricular conduction appeared from a few days to a few months subsequent to the experiment.

Three cases, in addition to impairment of auriculoventricular conduction, showed delay in intraventricular conduction time. Atropine had no effect on this disturbance.

In fifteen patients receiving aspirin at the time of study, nineteen observations were made (Table IV). When compared with the group of seven patients who had received no aspirin (Table V), it was found that the only essential difference was in the initial ventricular rate and its degree of acceleration following the injection of atropine. While the initial ventricular rates in the group which had not received aspirin were higher, on the average, than in the group which had (100.6 beats per minute as compared with 82), the average initial P-R intervals were practically identical (0.238 and 0.245 sec.). Following the injection of atropine, the average decrease in auriculoventricular conduction in the untreated group was 0.072 sec., with an average maximum acceleration in the ventricular rate of 33.7 beats per minute. The average decrease in the P-R interval of the group receiving aspirin was found to be 0.07 sec., with an average increase in the ventricular rate of 23.6 beats per minute.

TABLE IV

EFFECT OF INTRAVENOUS INJECTION OF ATROPINE SULPHATE UPON THE AURICULOVENTRICULAR CONDUCTION TIME IN PATIENTS WITH ACUTE RHEUMATIC FEVER WHILE RECEIVING ASPIRIN

NAME	AGE	SEX	CONTROL		AFTER ATROPINE INJECTION				CHANGE AFTER ATROPINE		SEDIMENTATION RATE
			VENTRICULAR RATE	P-R INTERVAL (SEC.)	DOSE OF ATROPINE (MG.)	TIME OF MAXIMUM CHANGE (MIN.)	MAXIMUM CHANGE		VENTRICULAR RATE	P-R INTERVAL (SEC.)	
							VENTRICULAR RATE	P-R INTERVAL (SEC.)			
I. M.	20	F	65	0.22	1.8	15	120	0.14	55	0.06	76
J. S.	25	M	80	0.22	1.5	3	95	0.18	15	0.04	50
			70	0.24	2.0	8	90	0.18	20	0.06	48
			75	0.22	1.8	1	90	0.17	15	0.05	23
J. W.	13	F	80	0.24	1.8	15	100	0.17	20	0.07	50
J. F.	41	M	85	0.28	2.0	1	100	0.22	15	0.06	70
			80	0.25	2.4	4	85	0.19	5	0.06	--
			70	0.22	2.4	4	90	0.16	20	0.06	70
L. S.	38	F	90	0.24	2.0	3	105	0.18	15	0.06	130
S. E.	40	M	70	0.23	2.0	1	100	0.18	30	0.05	--
H. L.	35	F	90	0.21	2.0	2	135	0.16	45	0.05	35
M. C.	28	F	85	0.32	2.0	3	116	0.20	31	0.12	50
J. H.	15	F	90	0.22	1.5	1	110	0.17	20	0.05	--
A. S.	25	F	90	0.24	1.5	10	110	0.17	20	0.07	27
A. C.	9	M	108	0.23	1.0	5	135	0.15	27	0.08	--
A. S.	34	F	75	0.28	2.0	7	110	0.20	35	0.08	37
G. W.	23	F	105	0.33	2.0	1	100	0.16	-5	0.17	70
L. C.	20	F	70	0.24	2.0	4	105	0.18	35	0.06	85
G. P.	15	F	100	0.23	1.8	10	130	0.16	30	0.07	130
Average	25.4			0.245				0.175	23.6	0.07	

TABLE V

EFFECT OF INTRAVENOUS INJECTION OF ATROPINE SULPHATE UPON THE AURICULOVENTRICULAR CONDUCTION TIME IN PATIENTS WITH ACUTE RHEUMATIC FEVER NOT RECEIVING ASPIRIN

NAME	AGE	SEX	CONTROL		AFTER ATROPINE INJECTION				CHANGE AFTER ATROPINE		SEDIMENTATION RATE
			VENTRICULAR RATE	P-R INTERVAL (SEC.)	DOSE OF ATROPINE (MG.)	TIME OF MAXIMUM CHANGE (MIN.)	MAXIMUM CHANGE		VENTRICULAR RATE	P-R INTERVAL (SEC.)	
							VENTRICULAR RATE	P-R INTERVAL (SEC.)			
C. L.	13	M	50	0.33	2.0*	10	75	0.23	25	0.10	60
H. B.	20	M	105	0.20	2.0	1	150	0.13	45	0.07	18
J. D.	13	M	125	0.20	1.5	7	165	0.14	40	0.06	57
			140	0.24	1.5	1	165	0.19	25	0.05	57
			95	0.22	0.5	3	145	0.17	50	0.05	--
M. C.	28	F	95	0.20	2.0	15	160	0.12	65	0.08	--
J. H.	15	F	125	0.23	1.5	3	135	0.16	10	0.07	--
B. B.	42	M	70	0.24	2.0	10	85	0.20	15	0.04	--
E. F.	38	F	100	0.28	1.5	10	128	0.15	28	0.13	--
Average	24.1		100.6	0.238			134.2	0.167	33.7	0.072	

*Intramuscular injection of the drug.

Thus, while the initial ventricular rate was higher in the group which did not receive aspirin, the increase which followed atropinization was also greater, by 20 per cent, than in the group of patients who had been given aspirin. The change in auriculoventricular conduction was the same for both groups. It would seem, therefore, that the administration of aspirin to this group of patients with acute rheumatic fever tended (1) to lower the cardiac rate; (2) to diminish the degree of response of the ventricular rate to atropinization. There was no apparent effect upon auriculoventricular conduction.

Influence of Emotion.—In all cases control electrocardiograms were taken about one hour prior to the start of the experiment. These tracings were developed and read in order to be sure of the presence of an auriculoventricular conduction defect. Second control electrocardiograms were taken just before the injection of atropine sulphate. In most of the cases, the explanation of what was being done, as well as the actual performance of the procedure, was unattended by any subjective discomfort. Three individuals, however, manifested some degree of fear and anxiety, either by tears or vocal protests. The second control electrocardiograms, when taken on these patients, showed marked decrease in auriculoventricular conduction, with little or no change in ventricular

TABLE VI

EFFECT OF EMOTION UPON THE AURICULOVENTRICULAR CONDUCTION TIME IN A PATIENT WITH ACUTE RHEUMATIC FEVER

E. F., Female, Aged 38 Years. Mitral Stenosis and Insufficiency. U. H. 444414

DATE 1935		TIME	VENTRICULAR RATE	P-R INTERVAL (SEC.)	REMARKS
March 9		9:50	90	0.16-0.32	
March 30		10:05	95	0.27	
April 1		11:10	115	0.27	
April 3	*Control*	9:58	100	0.28	Patient quite apprehensive when procedure was explained to her
	Control	10:50	95	0.16	
		10:55			Atropine 1.5 mg. intravenously
		10:56	128	0.14	
		11:00	118	0.14	
		11:05	115	0.13	
		11:10	110	0.14	
		11.12			Mouth dry
		11:25	118	0.14	
		11:55	100	0.15	
		12:55	108	0.14	
		1:55	100	0.15	
		2:55	100	0.15	
		3:55	98	0.18	
		4:55	100	0.28	
April 4		9:48	100	0.28	
April 5		10:50	96	0.28	
April 17		11:35	90	0.18	
April 25		10:50	80	0.17	

rates. Atropine was then injected in the usual way, and a further decrease in the P-R interval was obtained. In Table VI is given one of these protocols.

Epinephrine.—It seemed possible that the changes in auriculoventricular conduction which occurred during the period of emotional tension might be due to depression of the vagal influence by excitation of the sympathetic nerves to the heart. In an effort to reproduce this effect, epinephrine, in varying doses, was administered subcutaneously to five patients with acute rheumatic fever who showed a conduction defect by the electrocardiogram (Table VII). In all of these cases the prolonged

TABLE VII

EFFECT OF THE SUBCUTANEOUS INJECTION OF EPINEPHRINE HYDROCHLORIDE (1:1000) UPON THE AURICULOVENTRICULAR CONDUCTION TIME IN PATIENTS WITHOUT HEART DISEASE

NAME	DATE (1936)	TIME	AGE	SEX	CONTROL		ADRENALIN GIVEN (MIL.)	TIME AFTER INJECTION (MIN.)	MAXIMUM CHANGE	
					VENTRICULAR RATE	P-R INTERVAL (SEC.)			VENTRICULAR RATE	P-R INTERVAL (SEC.)
M. J.	June 9		35	F	100	0.13	0.5	8	+20	-0.03
H. A.	July 9	2:25	23	M	85	0.15	0.5	10	+ 8	0.00
		2:47			90	0.15	0.5	5	+ 2	0.00
W. B.	July 8	2:16	24	M	70	0.14	0.5	3	+ 5	-0.01
		2:39			72	0.14	1.0	20	+12	-0.02
M. F.	June 9	2:48	35	F	75	0.16	0.5	5	+18	-0.04
		3:05			75	0.15	1.0	4	+25	-0.08*

*Ectopic auricular rhythm.

P-R intervals were shown to be susceptible to atropine. A control group of four individuals who showed no evidence of heart disease or electrocardiographic abnormalities was similarly treated (Table VIII).

As can be seen, the injection of relatively small doses of epinephrine produced a slight acceleration of the ventricular rate, which averaged 11.2 beats per minute in the rheumatic, as compared with 12.8 in the control group. The change in the P-R interval was also practically identical in the two groups, 0.018 sec., in the rheumatic and 0.02 sec., in the control group.

When a second dose of epinephrine was administered subcutaneously 20 minutes after the first injection, wide variations in the effect on rate and conduction were observed. In the control group ventricular acceleration was again obtained, but not to a marked degree, averaging 13 beats to the minute. The decrease in conduction averaged 0.03 sec. with a range of 0.00 to 0.07 sec. In the case which showed the maximum fall, there was a change from the regular sinus mechanism to an ectopic auricular rhythm. In the rheumatic group, two cases showed a decrease

TABLE VIII

EFFECT OF EPINEPHRINE HYDROCHLORIDE (1:1000), INJECTED SUBCUTANEOUSLY, UPON THE AURICULOVENTRICULAR CONDUCTION TIME IN PATIENTS WITH RHEUMATIC HEART DISEASE

NAME	DATE (1936)	TIME	AGE	SEX	CONTROL		ADRENALIN (MIL.)	TIME AFTER INJECTION (MIN.)	MAXIMUM CHANGE		CHANGE IN SYSTOLIC B.P. FROM CONTROL (MM. HG)
					VENTRICULAR RATE	P-R INTERVAL (SEC.)			VENTRICULAR RATE	P-R INTERVAL (SEC.)	
A. C.	June 22	3:40	9	M	118	0.25	0.3	3	+ 7	-0.02	
		4:03			115	0.24	0.5	10	+20	-0.03	
A. S.	April 23	10:39	34	F	72	0.23	0.5	21	+18	0.00	- 6
		11:05				0.23	1.0	7	-25	*	+54
G. W.	May 19	11:00	23	F	88	0.33	1.0	15	+12	-0.04	+10
		11:17			100	0.29	1.0	8	0	-0.11†	+26
L. C.	Jan. 16	3:26	20	F	70	0.24	0.5	4	+12	-0.01	+15
	Jan. 18	9:10			75	0.21	1.0	4		*	+54
G. P.	July 29	11:19	15	F	75	0.24	0.5	18	+ 7	-0.02	+ 6
		11:38			82	0.22	0.5	16	+ 8	+0.06	+52

*Complete heart-block.
†Ectopic auricular rhythm.

in the P-R interval. In one, with a shortening of 0.03 sec., the ventricular rate increased 20 beats. In the second, with a shortening of 0.11 sec., there was no change in ventricular rate. The remaining three cases all showed an increase in conduction time. In two of these, transient, complete heart-block was observed. In all cases, numerous premature beats, of both nodal and ventricular origin, as well as shifting of the pacemaker, were observed. These effects were temporary, and the electrocardiogram returned to its original form within twenty minutes after the second injection of epinephrine.

It is well known that acceleration of the heart rate due to epinephrine results from stimulation of the endings of the accelerator nerves in the heart muscle; this is the characteristic feature of the action of epinephrine. With large amounts, acceleration may be temporarily replaced by retardation (Table IX). "This second phase of slowing is not observed if the vagi are divided or if atropine is given before adrenalin, so that it obviously arises from excitation of the vagus center. This is not mainly a direct adrenalin action but is largely a secondary result of the high blood pressure, which induces congestion of the brain and arouses the vagal center to activity. After a short time, the blood pressure beginning to fall, or the vagus center becoming exhausted, the accelerator stimulation again gains the upper hand."[6]

It may be possible, then, that the changes in rhythm observed in this series of rheumatic subjects following injection of the larger amounts of epinephrine are an expression of a hyperirritable vagal center. This

TABLE IX

EFFECT OF SUBCUTANEOUS INJECTION OF EPINEPHRINE HYDROCHLORIDE (1:1000) UPON THE VENTRICULAR RATE AND AURICULOVENTRICULAR CONDUCTION TIME IN A PATIENT WITH ACUTE RHEUMATIC FEVER

L. C. Female. Age 20. Mitral Stenosis and Insufficiency. U.H. 474067

DATE 1936		TIME	AURICULAR RATE	VENTRICULAR RATE	P-R INTERVAL (SEC.)	BLOOD PRESSURE	REMARKS
January 18	*Control*	9:05		75	0.21	102/58	
		9:10					Epinephrine 1 c.c.
		9:11		100	0.18	104/58	
		9:12		110	0.18		
		9:13				122/70	
		9:14	*100	75			
		9:15				160/94	
		9:17		96	0.18-0.34		
		9:18				166/88	
		9:20		85	0.21-0.22		
		9:21				150/72	
		9:24				134/74	
		9:25		80	0.21		
		9:27				126/70	
		9:30		82	0.21-0.22	120/60	
January 20		10:10		70	0.20	108/70	
January 21		10:20		60	0.20	117/70	
January 30		10:20		90	0.18	122/70	
February 11		2:45		70	0.18	120/80	
February 19		9:55		90	0.18	125/82	
February 28		10:25		98	0.18-0.19	118/76	
March 11		10:43		100	0.18	112/86	

*Complete heart-block.

explanation suggests that the source of vagal hypertonia may be not in the heart but in the medulla oblongata. Further evidence in support of this hypothesis is being sought.

Four of the rheumatic patients complained of transient, moderately severe, nonradiating precordial pain, occurring from twelve to fifteen minutes after the injection of the second dose of epinephrine. The increase in blood pressure was at its height at this time. An ice bag placed on the precordium was effective in controlling the pain, which never lasted more than several minutes. This symptom was not encountered in the control group, despite administration of comparable doses of epinephrine.

Exercise.—Observations on the effect of exercise upon prolonged auriculoventricular conduction time did not yield conclusive results. Only two patients were studied. The exercise consisted of sitting up and lying back in bed fifty times. In one case there was an increase in ventricular rate of 3 beats per minute, with a reduction of the P-R interval from 0.23 to 0.21 sec. (Table II). In the other case there was an increase in the cardiac rate of 4 beats per minute, with a fall in conduction time from 0.28 to 0.25 sec.

COMMENT

Loewi[7] has demonstrated that the vagus nerve does not act directly on the heart muscle. His evidence is simple and direct. Two frog hearts were isolated, one with its vagus nerve, the other without. Both hearts were filled with a small amount of Ringer's solution. The vagus nerve to the one heart was stimulated continuously for a few minutes and then the Ringer's solution from this heart was placed within the other. The second heart reacted as if its own vagus had been stimulated. If this second heart had previously been atropinized, no effect was exerted by the transferred fluid. Therefore, excitation of the vagus nerve produced or increased in amount a chemical substance which brought about slowing of the heart. This substance, which he called *Vagusstoff*, he was later able to prove to be, in all probability, identical with acetylcholine.[8]

Atropine counteracts the effect of vagal stimulation. It has been shown that the impairment of auriculoventricular conduction in these cases of acute rheumatic fever was temporarily diminished or abolished by the injection of atropine. It appears, therefore, that the conduction defect is caused, at least in part, by an increase in vagal tone. The significance of this fact is enhanced by the observations of Hall, Ettinger, and Banting.[9] These investigators injected eight dogs with a 1:10,000 solution of acetylcholine daily over a period of months. All of the animals died with terminal signs of cardiac failure. Examination of the hearts at necropsy showed severe damage to the myocardium and coronary arteries.

Attempts have been made to reproduce lesions in the myocardium and coronary arteries by vagal stimulation, similar to those achieved with the use of acetylcholine. These have not been successful.[10] Experiments on animals are being conducted in this laboratory along similar lines.

SUMMARY

Impairment of the auriculoventricular conduction time was studied in twenty-two patients with acute rheumatic fever. Observations were made (1) after the intravenous injection of atropine sulphate, (2) during a period of acute emotional stress, (3) following the subcutaneous administration of epinephrine hydrochloride, and (4) after exercise.

Atropine completely abolished the conduction defect in nineteen of the twenty-two cases studied. There was a marked diminution in the degree of block in the one case in which the drug was given intramuscularly. The effect was always transient. Since acceleration in ventricular rate did not necessarily parallel decrease in conduction time, it appears that these two effects are not directly related. In one of the two cases which did not show a reduction in the degree of block after atropinization, the impairment persisted for a year and was probably due to organic changes

in the junctional tissues. Three cases, in addition to impairment of auriculoventricular conduction, also showed delay in intraventricular conduction. Atropine had no effect on this disturbance.

In three individuals, who gave evidence of emotional stress at the time of the observations, marked reduction in the P-R intervals was noted, despite little or no acceleration of ventricular rate.

Small doses of epinephrine, injected subcutaneously, in five cases produced a result similar to that observed in a control group. Larger dosage, however, exerted two opposite effects; it either diminished the conduction defect (two cases), or markedly increased it (three cases). The latter result was not seen in a control group under similar conditions.

After moderate exercise, there was some decrease in the P-R interval, with slight increase in ventricular rate.

It is concluded that, in cases of acute rheumatic fever, impairment of auriculoventricular conduction is due, in part at least, to an increase in vagal tone. The significance of this fact is briefly discussed. It is suggested that the focus of vagal irritation lies in the medulla.

REFERENCES

1. Parkinson, J., Gosse, A. H., and Gunson, E. B.: The Heart and Its Rhythm in Acute Rheumatism, Quart. J. Med. **13**: 363, 1920.
2. Swift, H. F.: Rheumatic Fever, Am. J. M. Sc. **170**: 631, 1925.
3. Rothschild, M. A., Sachs, B., and Libman, E.: The Disturbances of the Cardiac Mechanism in Subacute Bacterial Endocarditis and Rheumatic Fever, AM. HEART J. **2**: 356, 1927.
4. Levy, R. L., and Turner, K. B.: Impaired Auriculoventricular Conduction in Rheumatic Fever, Arch. Int. Med. **43**: 267, 1929.
5. Lewis, T., Drury, A. N., and Iliescu, C. C.: Some Observations Upon Atropine and Strophanthin, Heart **9**: 21, 1921.
6. Cushny, A. R.: Pharmacology and Therapeutics, ed. 7, Philadelphia, 1918, Lea and Febiger, p. 368.
7. Loewi, O.: Ueber humorale Uebertragbarkeit der Herznervenwirkung, Pflügers Arch., V **189**: 239, 1921.
8. Loewi, O.: The Humoral Transmission of Nervous Impulse, Harvey Lectures, 1932-1933, Series 28, p. 219.
9. Hall, G. E., Ettinger, G. H., and Banting, F. G.: An Experimental Production of Coronary Thrombosis and Myocardial Failure, Canad. M. A. J. **34**: 9, 1936.
10. Ettinger, G. H., Hall, G. E., and Banting, F. G.: Effect of Repeated and Prolonged Stimulation of the Vagus Nerve in the Dog, Canad. M. A. J. **35**: 27, 1936.

DISSECTING ANEURYSM OF THE AORTA, CORRECTLY DIAGNOSED

With Description of a Sign Heretofore Not Mentioned*

H. Roesler, M.D., U. G. Gifford, M.D., and W. Betts, M.D.
Philadelphia, Pa.

Case History.—J. B., male, aged seventy-five years, was supposed to have had typhoid fever at the age of sixty years. Six months ago he felt well. His blood pressure at that time was 180/95, and the urine showed a trace of albumin. Progressive shortness of breath developed during the last two months.

On the evening of May 24, 1936, he ate a heavy meal and immediately afterward carried a heavy pail for thirty yards. Ten minutes later, while standing and talking to a neighbor, he was suddenly seized with a severe pain in the back of his neck and upper dorsal region. The pain became more severe lower down the back and under the lower sternum. There was no radiation into the arms. He walked to his house, upstairs to his room, and became gray and perspired. Vomiting was induced but brought no relief. He was very restless and walked from room to room.

He was given morphine and admitted to the hospital on the next evening. His blood pressure was 165/140 in the right arm and 180/140 in the left arm. The heart was enlarged to the left, and there was a wide, heaving apical impulse. There was a mitral systolic murmur and a well-marked protodiastolic gallop rhythm. The aortic second sound was greatly accentuated; no murmurs were heard. Both lung bases were full of moist râles, and bloody, frothy mucus was raised. The temperature was 99° F. The heart rate was regular, 104 per minute, but the next day premature ventricular beats were heard, and short runs of tachycardia, thought to be of ventricular type, appeared. The pulmonary edema cleared up. The blood pressure remained constantly elevated, 165 to 240 systolic and 118 to 140 diastolic. The temperature did not exceed 100° F. Pain, requiring relief by morphine or dilaudid, continued for five days.

On the ninth day a pulsating area was discovered in the left interscapular area, at the level of the eighth interspace, the center being 6 cm. from the spinous processes. Three days later it was found to be 9 cm. out. Over this pulsating area the aortic second sound was very accentuated. On the fifth day of this illness he complained of pain in the lower dorsal and upper lumbar region.

Laboratory Findings.—The leucocyte count varied from 10,000 to 15,000. The urine showed albumin but no casts, with a specific gravity of 1.025. Blood urea nitrogen was 9 mg. per 100 c.c. Electrocardiograms were taken on the third and fifth days of his illness. There was present an isoelectric T_1, left axis deviation on the second occasion, and a few premature auricular beats. The first bedside roentgenograms were taken on the eleventh day following the attack. There was an aortic configuration with enlargement downward and to the left. There was a definite widening of the supra-aortic shadow in the region of the right innominate artery. The aortic shadow appeared moderately widened, markedly elongated, with the descending aortic contour slightly convexly curved and prominent. The air content of the left lung field was diminished. The left anterior oblique view revealed a prominence of the

*From the Chester County Hospital, West Chester, Pa., and the Departments of Medicine and Roentgenology, Temple University School of Medicine, Philadelphia, Pa.

descending thoracic aorta dorsad, with poor definition of its contour because of the diminished contrast. The second bedside roentgenogram was taken seven days later, a few hours preceding the patient's death. A very marked, rather sharply defined, bulging prominence was noted in the cranial portion of the descending thoracic aorta. Its level coincided exactly with the area of pulsations in the left interscapular space.

Death occurred suddenly on the eighteenth day of the illness. The clinical diagnosis was hypertensive atherosclerotic cardiovascular disease with dissecting aneurysm of the aorta.

Post-Mortem Examination on June 11, 1936 (Dr. I. P. P. Hollingsworth). The heart weighed 490 grams. There was marked left ventricular hypertrophy and dilatation. The coronary arteries showed thickened walls, with plaques and diminished lumina. There was no evidence of thrombosis or infarction. The valves were normal. The entire thoracic aorta was moderately widened; the innominate artery was dilated, and its walls were thickened. The aorta, particularly the abdominal

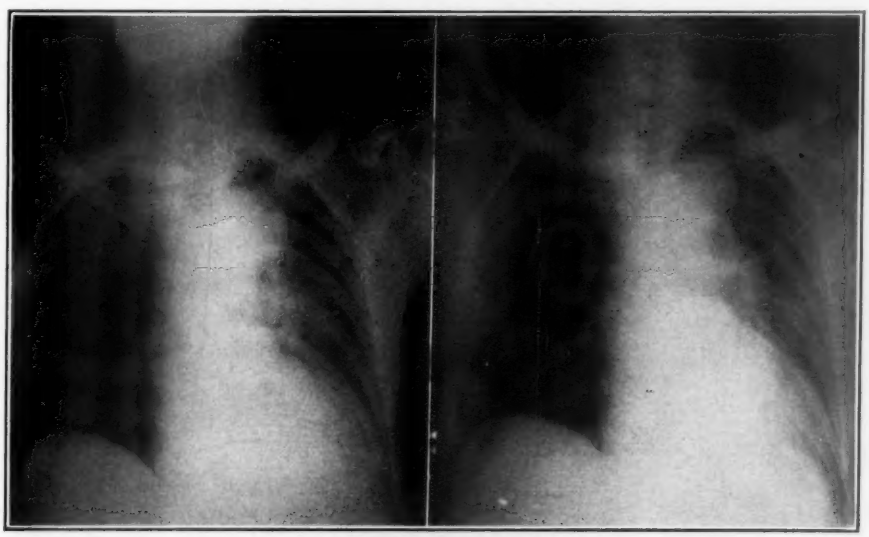

Fig. 1.—Roentgenograms, anteroposterior projection. The criteria for comparing correctly the two films are not completely fulfilled. The development of a bulging prominence in the course of the descending thoracic aorta, however, is clearly demonstrated. There is also a marked widening in the area which corresponds to the innominate artery.

portion and all main branches, showed advanced atherosclerotic changes with calcareous plaques. There were thrombi in both iliac arteries. At a point 15 cm. from the aortic valve was the beginning of a large dissecting aneurysm which extended downward for 15 cm. This area bulged distinctly, showed a dark discoloration, and the external coat of the aorta was thinned. On the lateral and posterior aspect a rupture 0.25 cm. long had occurred. The diameter of the aorta at the point of rupture was 7 cm., the average diameter of the aneurysmal sac 5.5 cm. The left pleural cavity was completely filled with blood. There was a hemorrhagic retroperitoneal infiltration at the left side, following the sheaths of the muscles, extending well up on the lateral abdominal wall. It was thought that this infiltration had occurred from the pleural cavity at the root of the diaphragm, no other aortic or arterial rupture having been found. The kidneys were slightly enlarged, with roughened surface. On section they were of pale pinkish color with poorly defined corticomedullary boundary.

Microscopic Study: Aneurysm—the muscular coats of the media were markedly separated by hemorrhagic infiltration. Kidneys—chronic glomerulonephritis and arteriosclerosis.

DISCUSSION

As to the clinical picture and the pathology of dissecting aneurysm, the reader is referred to the monograph of Shennan[1] and to the article of Weiss,[2] in which there are ample references.

In our case we considered in differential diagnosis cardiac infarction, pulmonary infarction, and dissecting aneurysm of the thoracic aorta.

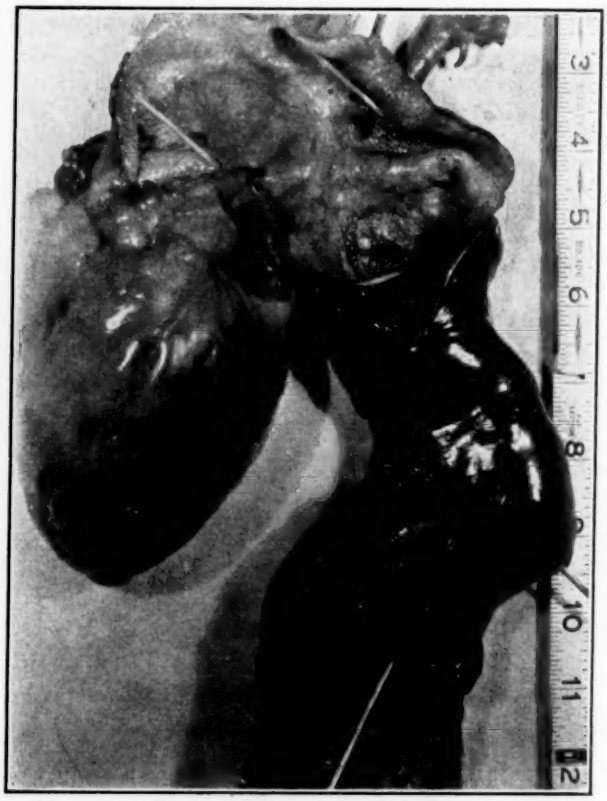

Fig. 2.—Post-mortem specimen. The lower probe leads into the lumen of the aorta. The probe to the right indicates the place where the dissecting aneurysm ruptured into the left pleural cavity.

The last diagnosis was established because of the type of pain, persistence of high blood pressure, absence of electrocardiographic changes characteristic for cardiac infarction. Full certainty was gained because an area of pulsation was observed to appear in the back and to move laterally. The second roentgenogram permitted a visualization of the rapid progression of the aneurysmal bulge at that level. It was not studied, however, until the patient had died and to this extent did not influence the already established diagnosis.

The observation of a rapidly shifting (increasing) area of pulsation, indicating the development of a dissecting aneurysm, has apparently not been reported before. In Wyss' case[3] there was a pulsating area present below the right clavicle. It increased slowly in the course of many weeks and the post-mortem examination revealed a dissecting aneurysm, 12 cm. in size, starting 6 cm. above the aortic valves. Such a slow increase may be found in connection with an aneurysm of the ordinary variety. In Bahrdt's case,[4] with correctly diagnosed dissecting aneurysm of the abdominal aorta, there was present a pulsating tumor the size of a hen's egg above the navel.

A number of recent articles dealing with proved cases of dissecting aneurysm of the aorta provide roentgenological descriptions, and most of them illustrations also.[2, 5-14] Kienböck and Weiss' case[21] is convincing but was not verified anatomically. In order to understand the varying roentgenological appearance, a very short anatomical discussion is needed. The size, extension, and amount of circular dissection vary greatly. Rupture near the aortic arch is common, and the dissection may travel distally or proximally. The newly formed blood path may almost completely encircle the aortic tube, thus forming a case or coat. More frequently only half to two-thirds of the circumference is involved. Thus it may come to lie essentially in a frontal or sagittal plane of the aortic vessel proper. The form may be either saccular-circumscript or, more often, cylindrical-diffuse.

A marked fluid collection in the pleural cavity or a diffuse extravasation of blood into the mediastinal tissues can easily interfere so that the roentgenological diagnosis becomes impossible. With the dissection extending between the brachiocephalic vessels or almost entirely encircling portions or the entire length of the thoracic aorta, the differentiation of a simple dilatation or cylindrical or saccular aneurysm of the thoracic aorta is impossible. An exception to this general statement must be made. The aorta may contain lime salt deposits, and its contour will then be visualized as a denser, linear shadow within a larger, usually cylindrical, but occasionally globular, and otherwise homogeneous shadow mass. If the newly formed aneurysm involves only a part of the circumference of the aortic vessel and has a predominantly lateral location, with respect to the direction of projection, it will be visualized as an outer, lighter shadow, usually of fairly even width, superimposed in a shell-like fashion upon the aortic shadow proper. The latter then appears as a more dense nuclear shadow, the size and shape of which is commonly, though not necessarily, altered in the sense of dilatation, fullness and tortuosity. Again, lime salt deposits may form a line of demarcation.

Dissecting aneurysm of the aorta has seldom been correctly diagnosed in the past, but this is changing recently. Thus Shennan[1] accepts six cases[3, 4, 5, 9, 15, 16] in his analysis of 300 cases up to and including 1932.

We reject one[3] but add another.[6] Since then there have been ten additional cases.[2, 7, 13, 14, 18, 19, 20] This, then, is the seventeenth case correctly diagnosed.

SUMMARY

A case with dissecting aneurysm of the thoracic aorta is reported in which the correct diagnosis was established.

A new diagnostic sign is described, consisting in the appearance of an area of pulsation which shifts rapidly; associated with it is the rapid change in the roentgenological appearance of the aortic shadow.

The roentgen findings in general are discussed.

The cases in which the diagnosis was correctly made are cited.

REFERENCES

1. Shennan, T.: Medical Research Council, Spec. Rep. Ser. No. 193, London, 1934, His Majesty's Stationery Office.
2. Weiss, S.: Med. Clin. North America **18**: 1117, 1935.
3. Wyss, O.: Arch. Heilk. **10**: 490, 1869.
4. Bahrdt, R.: Arch. Heilk. **13**: 473, 1872.
5. Davy, H., and Gates, M.: Brit. M. J. **1**: 471, 1922.
6. Hirschboeck, F. J., and Boman, P. G.: Minnesota Med. **5**: 724, 1922.
7. Patrick, C. V., and Taylor, J. F.: Lancet **1**: 181, 1929.
8. Tidmarsh, C. J.: Canad. M. A. J. **23**: 416, 1930. (See also Wood-Pendergrass-Ostrum.)
9. Barton, E. M.: Tr. Chicago Path. Soc. **13**: 399, 1930.
10. Wood, F. C., Pendergrass, E. P., and Ostrum, H. W.: Am. J. Roentgenol. **28**: 437, 1932.
11. Canigiani, Th.: Fortschr. a. d. Geb. Röntgenstrahlen **45**: 416, 1932.
12. Holzmann, M.: Acta radiol. **13**: 21, 1932.
13. Hamman, L., and Apperly, F. L.: Internat. Clin. **4**: 251, 1933.
14. Osgood, E. E., Gourley, M. F., and Baker, R. L.: Ann. Int. Med. **9**: 1398, 1936.
15. Swaine: Tr. Path. Soc., London **7**: 106, 1855, 1856.
16. Moosberger, W.: Schweiz. med. Wchnschr. **54**: 327, 1924.
17. Kellogg, F., and Heald, A. H.: J. A. M. A. **100**: 1157, 1933.
18. White, P. D., Badger, T. L., and Castleman, B.: J. A. M. A. **103**: 1135, 1934. (Footnote.)
19. Lounsbury, J. B.: Yale J. Biol. & Med. **7**: 209, 1935.
20. Löffler, W.: Schweiz. med. Wchnschr. **65**: 790, 1935.
21. Kienböck, R., and Weiss, K.: Fortschr. a. d. Geb. Röntgenstrahlen **44**: 212, 1931.

THE CLINICAL VALUE OF COMPARATIVE MEASUREMENTS OF THE PRESSURE IN THE FEMORAL AND CUBITAL VEINS*

EUGENE B. FERRIS, JR., M.D., CINCINNATI, OHIO, AND
ROBERT W. WILKINS, M.D., BOSTON, MASS.

THE USE of accurate methods for measuring systemic venous pressure has resulted in a definite increase of our knowledge of cardiac failure, particularly failure of the right ventricle. In addition, accurate measurements of venous pressure in both arms have been shown to be of value in locating lesions in the upper mediastinum which obstruct the superior vena cava, the innominate or the subclavian veins.[1, 2] When such lesions exist, however, the venous pressures as measured in the arms obviously are of no use in estimating the degree of heart failure. Villaret and Desoille[2] and others[3, 4] have demonstrated the importance of comparative determinations of venous pressure in both the arms and the legs when lesions press upon or obstruct the inferior vena cava. They have pointed out that in conditions such as pregnancy, ascites, and tumors of the abdomen, the pressure in the leg veins is high but is normal in the arm veins. Aside from these reports, the diagnostic importance of comparative venous pressure measurements has received little attention. The purpose of this paper is to demonstrate the clinical value of comparative observations of the pressure in the cubital and femoral veins and to describe instances in which puncture of the femoral veins has been partieularly useful.

FEMORAL VENEPUNCTURE

Puncture of the superficial veins of the legs may be difficult if not impossible, especially when there is edema or obesity. Puncture of the femoral vein, on the other hand, because of its constant position in relation to well-recognizable anatomical landmarks, is an easy procedure and has been used in several clinics for a number of years.[5, 6, 7] It may be used not only for the measurement of pressure in a vein draining directly into the inferior vena cava, but also for the removal and administration of blood or other fluids. In preparing to puncture the femoral vein, one locates the pulsation of the femoral artery in the groin below Poupart's ligament. The skin is cleansed with alcohol and an area just medial to the artery is infiltrated with novocaine. An 18 or 19 gauge needle, 1½ inches long, is then inserted through the skin and guided toward a point approximately 1 cm. medial to the maximal arterial pulsation; the needle should be directed upward and at an angle of about 60 degrees from the plane of the skin. By main-

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard University Medical School; and the Department of Internal Medicine, University of Cincinnati College of Medicine.

taining a slight negative pressure in the syringe, blood will appear the moment the vein is punctured. If the artery is continually palpated during this procedure, the position of the neighboring vein can be more accurately localized. Should the needle pass through or medial to the femoral vein, the pubic bone will be encountered. The femoral artery may be inadvertently punctured, but no harm will result if the needle is withdrawn and firm pressure maintained over the area for two or three minutes. The direction of the needle should not be changed while deep in the tissues because of the danger of tearing the arterial or venous wall. Solutions which are prone to cause thrombophlebitis should not be administered by this route.

METHOD OF MEASURING VENOUS PRESSURE

The direct method of Moritz and von Tabora[8] has been used to obtain venous pressures. A description of a simple and practical modification of this method for measuring the pressure in the cubital veins can be found elsewhere.[1] This method consists in using a graduated manometer connected by means of a three-way cock with a needle and a syringe containing normal saline solution. The pressure in the femoral veins can be obtained best by including a rubber tube between the manometer and the syringe, thus giving the system more flexibility. The patient should be placed in a horizontal position when possible, and it is essential that he be relaxed. The venous pressure as measured in the manometer is related to the manubrium sterni by means of a spirit level, and in turn to the right auricle by adding 5 cm. which is the average distance that the auricle lies below the manubrium. Our observations indicate that the normal venous pressure range is from 4 to 10 cm. of water, with an average of 6 cm. of water.

CLINICAL OBSERVATIONS

During the past two years we have routinely made comparative direct measurements of venous pressure in the femoral and cubital veins in cases in which the history or physical findings suggested the possibility of an elevation of venous pressure, due either to an obstruction or to questionable cardiac failure. The following examples illustrate the types of cases observed and the information obtained from venous pressure determinations.

CASE 1.—E. F., an eighty-eight-year-old woman, entered the Boston City Hospital complaining of mild dyspnea, weakness, and attacks of palpitation for one year. She had lost considerable weight. Examination revealed that she was dyspneic but not orthopneic. The neck veins were slightly distended. There was no tumor in the neck. The heart rate was 120 per minute, the rhythm grossly irregular, and the blood pressure 150/40. The peripheral pulse was bounding and the extremities were warm. There was no edema. The history of palpitation and loss of weight and the findings of warm extremities and a large pulse pressure suggested hyperthyroidism. Since the pressure was found to be 10.5 cm. of water in the cubital veins and only 5 cm. in the femoral veins, the diagnosis of a substernal thyroid with slight superior

caval obstruction was entertained. This was later confirmed by x-ray examination. The basal metabolic rate was +35 per cent. Because of her age and the danger of tracheal collapse, operation was rejected in favor of iodine and deep x-ray therapy. The basal metabolic rate came down to +17 per cent, and she was allowed to go home. Four months later she reentered the hospital with bronchopneumonia and empyema from which she died. Autopsy revealed a large adenomatous thyroid weighing 300 gm., which filled a large part of the upper mediastinum.

Differential venous pressures were of aid in determining the presence and the location of a mediastinal tumor in this case.

CASE 2.—C. H., a twenty-six-year-old male, entered the Boston City Hospital because of weakness, substernal oppression, dyspnea, cough, and hemoptysis for three weeks. There was no orthopnea. Physical examination revealed marked distention of the veins of the neck and arms, and dilatation of the superficial venules of the thorax. There was slight cyanosis of the face, lips, and fingernail beds. He had definite gynecomastia. There were signs of consolidation at the apex and of fluid at the base of the right lung. In addition to these findings, x-ray films showed the presence of several areas of density in the left lung. Although the syndrome of acute superior vena caval obstruction was fairly obvious in this case, the possibility of inferior caval obstruction or of superimposed cardiac embarrassment could not be entirely ruled out. The venous pressure was found to be 23.5 cm. of water in the right arm, 23 cm. in the left arm, and only 4.5 cm. in the femoral vein, clearly indicating a superior mediastinal obstruction involving the superior vena cava but not affecting the inferior cava or the cardiac function. The urine was later found to contain large amounts of prolan B, and in the absence of testicular abnormality a diagnosis of primary mediastinal chorionepithelioma was made. At autopsy the diagnosis was confirmed, and the location of the tumor was found to agree with the clinical impression. The mass completely filled the upper mediastinum, and tumor tissue had invaded the lumen of the superior vena cava, causing almost complete obstruction. The inferior vena cava was not involved either through encroachment or invasion by tumor tissue.

CASE 3.—N. H., a forty-five-year-old male, was admitted to the Cincinnati General Hospital complaining of progressively enlarging abdominal veins for two months. For two years previously he had had a chronic cough with moderate amounts of purulent sputum. During this period the diagnosis was thought to be either chronic lung abscess or encapsulated empyema because a small amount of pus had been obtained from the right chest by thoracentesis. Physical examination revealed an undernourished male, comfortable in bed with no orthopnea or dyspnea. The veins of the neck and arms appeared moderately distended and tense. A large plexus of dilated, tortuous veins was seen over the entire abdominal wall and lower part of the anterior chest (Fig. 1). The direction of flow was difficult to determine. The left lung was normal, but there were flatness and absence of breath sounds over the entire right lung, with some retraction of the trachea and heart to the right. The heart was essentially negative; blood pressure 132/86. The abdomen was negative to palpation. Both saphenous veins were prominent, but appeared thrombosed because no blood could be obtained from them. Venous pressure measurements at the time of admission were median cubital vein (both arms), 35 cm. of water; abdominal vein at center of plexus, 22 cm.; and femoral vein, 8.0 cm. X-ray studies showed a complete atelectasis of the right lung. Bronchoscopic examination demonstrated an occlusion of the right main stem bronchus at its bifurcation. Biopsy specimens were unsatisfactory, but a clinical diagnosis of advanced bronchogenic carcinoma was made. Before differential venous pressures were available, there was considerable discussion as to whether the patient had superior or inferior caval obstruction or both since the direction of blood flow in the abdominal veins

was difficult to determine. The value of these determinations in localizing the lesion in the upper mediastinum is obvious. It should be pointed out that the appearance of anastomosing abdominal veins does not help in differentiating superior from inferior caval obstruction as the same veins are involved in either case.

The patient died four months after admission to the hospital. Autopsy showed extensive carcinoma which appeared to be primary in the right main stem bronchus, where it caused complete occlusion. The entire right lung was inelastic and filled with multiple small abscess cavities. The growth had extended to the superior vena cava, which was completely occluded from its entrance into the right auricle to a

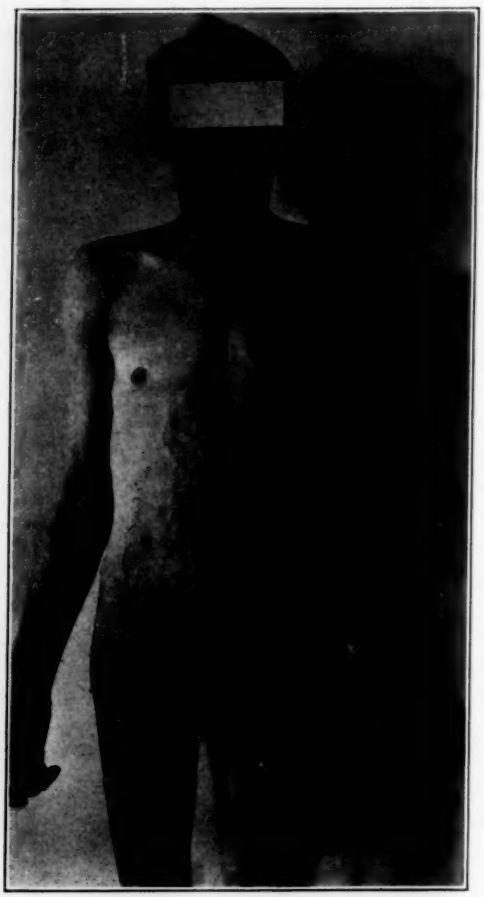

Fig. 1.—Photograph of N. H. (Case 3) showing the venous anastomosis which resulted from superior vena caval obstruction.

point about 1 cm. below its bifurcation into the innominate veins. The inferior vena cava was patent throughout. It is of interest that in both this and the preceding case the caval obstruction was brought about by extension of the tumor into the lumen of the vein.

CASE 4.—H. C., a thirty-four-year-old male, entered the Boston City Hospital complaining of increasing dyspnea, hoarseness, and cough with small amounts of whitish sputum for two months. For two weeks he had been unable to sleep at night because of orthopnea and attacks of smothering. He also complained of a constant

dull substernal ache of ten days' duration. Examination revealed a well-nourished man with moderate cyanosis and severe respiratory distress of Cheyne-Stokes character. There was engorgement of the veins of the neck and arms and distention of the venules on the anterior chest. There was nothing remarkable about the leg veins. Except for moist râles at both bases, the lungs were clear. The left border of the heart was 11 cm. from the midsternal line, while the right border was at the sternal margin. There was a gallop rhythm but no murmurs. The heart rate was 110; rhythm, regular; blood pressure, 110/80. The abdomen, extremities, and reflexes were normal.

On the basis of the history and physical signs, suggesting a substernal lesion obstructing the superior vena cava, involving the recurrent laryngeal nerve, and embarrassing the heart and respiration, a provisional diagnosis of an upper mediastinal tumor was made. Simultaneous direct venous pressure determinations revealed a pressure of 17.5 cm. in both the femoral and cubital veins. This finding definitely ruled out a single upper mediastinal lesion and proved that the difficulty was cardiac in origin, either pericardial, myocardial, or endocardial, or a combination of these. An electrocardiogram showed left bundle-branch block and T-wave changes of severe myocardial disease. Fluoroscopy revealed no evidence of pericardial effusion or adhesions. With rest in bed the patient improved and venous pressures dropped to 9.5 cm. in both arms and legs. The etiology of the myocarditis remained obscure.

This case illustrates the fact that mere inspection of the veins, especially the leg veins, is of little value in estimating the venous pressure. It also demonstrates the necessity of comparative venous pressures, not only in the arms, but also in the legs in order to rule out superior caval obstruction and to establish the diagnosis of cardiac decompensation.

CASE 5.—J. D., a fifty-two-year-old male, entered the Boston City Hospital complaining of intermittent smothering sensations, hoarseness, and pain in the left shoulder for three years, and of painful swelling and contracture of the fingers of the left hand for two months. Physical examination revealed a well-nourished, apprehensive man, comfortable when flat in bed. At times he talked in a hoarse voice and he also had an intermittent dyspnea in bed. Heart, lungs, and abdomen were normal. There was marked limitation of motion of the left shoulder with spasm of the pectoral muscles. The fingers of the left hand were contracted and cyanotic, and the hand was moderately edematous. Some observers thought the left arm veins were distended. Direct venous pressures were the same, 9.5 cm. of water in both of the cubital and the femoral veins. This definitely ruled out a venous obstruction as the cause of the complaints in the left arm and hand and also cast grave doubt on the presence of a substernal lesion as a cause of his hoarseness and smothering. It developed that he had been known for years, by many hospital admissions, as a hysterical individual. He had lately been selling medical books which he had read, with the result that he had a surprising store of odd medical facts. X-ray films revealed hypertrophic arthritis of the left acromioclavicular joint. Laryngoscopy showed a normal larynx. With orthopedic treatment and strong psychotherapy his symptoms subsided.

CASE 6.—E. W., a fifty-six-year-old male, entered the Cincinnati General Hospital complaining of swelling of the legs for three months, dyspnea on exertion for two months, and nocturnal attacks of dyspnea for three weeks. Ten months before this admission he had had a transurethral prostatic resection for the relief of urinary retention. A biopsy at that time revealed carcinoma of the prostate. Physical examination showed a poorly nourished male propped up in bed, with rapid, but not

labored, respirations. The veins of the arms were distended but appeared to collapse at a normal distance above heart level. Percussion revealed the left border of the heart 14 cm. from the midsternal line. The rhythm was regular, and there were no significant murmurs. The blood pressure was 128/92. There were signs of bilateral hydrothorax. The liver was not felt. There was marked edema of the legs and trunk. In the left scrotum there was a fluctuant swelling about 10 cm. in diameter. Numerous enlarged firm nodes were palpated in both inguinal regions. On rectal examination a large irregular mass was felt anteriorly.

Because of the history of dependent edema, dyspnea on exertion, and paroxysmal nocturnal dyspnea, the patient was thought on admission to have congestive failure independent of prostatic carcinoma and was treated with digitalis and diuretics. Also 600 c.c. of fluid were removed from the left chest and 650 c.c. from the right. This fluid had the character of a transudate. These procedures relieved the dyspnea out of proportion to the edema which was still marked ten days after admission. Venous pressures at this time were 5 cm. of water in the cubital veins, 29 cm. in the right femoral vein, and 23 cm. in the left femoral vein.

X-ray studies revealed infiltrative lesions throughout both lung fields and extensive bone metastases, both osteoclastic and osteoblastic in nature. Laboratory studies showed a secondary anemia, a negative blood Kahn reaction, and a total serum protein of 8.7 grams per 100 c.c.

The venous pressures in this case clearly established the presence of a local venous obstruction as the principal cause of the edema of the lower part of the body. Together with the x-ray findings, they also made it fairly certain that the lung metastases and pleural effusions, rather than cardiac failure, were responsible for the dyspnea.

CASE 7.—M. Q., a fifty-year-old male, entered the Boston City Hospital because of ascites and edema of the legs which resulted from alcoholic cirrhosis of the liver, later proved at autopsy. The abdominal fluid reaccumulated so rapidly that frequent abdominal taps were necessary. Simultaneous determinations of the venous pressure in the cubital and femoral veins were made before and after removal of the fluid on eight occasions. Depending on the tenseness of the abdominal wall, the femoral venous pressures, before tapping, ranged from 17 to 24.5 cm. of water. After removal of as much fluid as possible they fell to from 10 to 12 cm. of water. The pressure in the median cubital vein was unaffected by removal of the fluid and remained at a normal level of 7 to 8 cm. of water. Further observations demonstrated that the height of the pressure in the femoral vein was directly related to the intra-abdominal pressure. When a few hundred cubic centimeters of fluid were removed, there was a drop in venous pressure out of proportion to the amount of fluid removed. This initial drop coincided with a relaxation of the anterior abdominal wall, and thereafter the venous pressure appeared to equal the hydrostatic pressure of the ascitic fluid alone. Thus when a manometer was attached to the paracentesis trocar the ascitic fluid rose several inches within the tube only as long as the abdominal wall was tense. Correspondingly, the pressure in the femoral vein approximated the level to which this fluid rose. As fluid was removed, the excessive tension on the abdominal wall was quickly relieved, and the fluid level fell below the trocar, while the venous pressure likewise fell rapidly. Thus, in ascites, the intra-abdominal and femoral venous pressures depend in part on the tension of the abdominal wall as well as on the actual amount of fluid present.

CASE 8.—E. H., a fifty-year-old woman, entered the Boston City Hospital complaining of painless swelling of the abdomen for one year. There was mild dyspnea on exertion but no orthopnea or any other complaint. The past history was entirely negative. Physical examination showed a well-nourished woman comfortable flat in bed with slight cyanosis and marked distention of the neck veins. The lungs were clear except for high diaphragms and atelectatic râles at the bases. The heart was of

normal size, the sounds of good quality, with a reduplicated second sound at the apex, but no murmurs. The rate and rhythm were normal. The blood pressure was 135/80. The abdomen was markedly distended with fluid, and the liver edge was felt 8 cm. below the rib margin. There was slight pitting edema of the lower legs. Laboratory studies revealed normal blood and normal kidney and liver function. The Takata-Ara tests on blood and ascitic fluid were negative. The electrocardiogram was normal. Fluoroscopy revealed slightly decreased pulsations of the heart, but otherwise no abnormality.

The abdomen was repeatedly tapped to remove the rapidly reaccumulating fluid which had the characteristics of a transudate. Venous pressures immediately before the abdominal tap were 34 cm. of water in the femoral veins and 33 cm. in both median cubital veins. Immediately after the removal of 9.5 liters of fluid the venous pressures were 20 cm. in the femoral veins and 18 cm. in the cubital veins. After the tap the vital capacity rose from 1,600 to 2,000 c.c. As the fluid reaccumulated, the venous pressures gradually returned to their previous levels.

The clinical picture was that of an active woman, free of symptoms except for swelling of the abdomen, with the peripheral signs of severe right-sided heart failure. The venous pressures proved that the difficulty was cardiac, and in the absence of significant signs of valvular or myocardial disease suggested constrictive pericarditis. She was seen in consultation by Dr. Elliott C. Cutler, who agreed to operate. At operation a dense tough pericardium, 3 mm. thick, was found adherent to the heart everywhere by tough adhesions, causing constriction. The pericardium was excised from the heart on all sides down to the venae cavae. She went through the three-hour procedure in excellent condition with pulse and blood pressure unchanged. The venous pressures throughout fell from a preoperative level of 18 cm. of water to 8 cm. of water postoperatively.

This case illustrates the value of comparative venous pressure determinations in both the arms and the legs in ruling out cirrhosis of the liver and in establishing the presence of a lesion embarrassing the heart. The fall in venous pressures as well as the rise in vital capacity after the removal of abdominal fluid in this case was interpreted as the result of the improved cardiac and respiratory function with the release of the intrathoracic pressure due to high diaphragms. Exactly the same observations were made in a second case of constrictive pericarditis diagnosed clinically but not proved by operation or autopsy.

CASE 9.—R. N., a thirty-six-year-old male, was admitted to the Boston City Hospital with a history of drinking one-half pint of alcohol a day for two years and a pint to a quart a day for three months. He had eaten a grossly inadequate diet which became more deficient, the more he drank. He complained of increasing dyspnea for one month, dependent edema for three weeks, cough for ten days, and orthopnea with sleeplessness for one day. Examination revealed an apparently well-nourished man with severe orthopnea and massive edema of every dependent part. The skin of the hands and lower legs showed typical pellagrous scaly pigmentation. The neck veins were engorged. There were signs of congestion over the lower one-third of both lungs. The heart was enlarged to the right and left, and there was a blowing systolic murmur with a gallop rhythm. The heart rate was 120 per minute and the blood pressure 110/50. The liver was palpated 4 cm. below the costal margin, but the spleen was not felt. Knee jerks were greatly diminished, and ankle jerks were absent. Laboratory studies revealed normal blood except for moderately lowered serum proteins: total protein, 5.2 gm. per 100 c.c. plasma; albumin, 2.92 gm.; and globulin, 2.28 gm. The Takata-Ara test on the blood was negative. Venous pressures in both arms and legs were 26 cm. of water and rose on the third day to 32 cm. On this day the patient suddenly went into circulatory collapse and died. Post-mortem

examination revealed marked dilatation of the right heart, and microscopic sections showed edema of the myocardium, both findings said to be typical of beriberi heart disease.[9]

The history and presenting symptoms in this case might suggest a protein-deficiency type of edema. The abnormal venous pressures clearly demonstrated the presence of myocardial failure, confirmed at autopsy as the chief cause of death.

CASE 10.—S. M., a forty-year-old male, entered the Boston City Hospital complaining of increasing edema, dyspnea, orthopnea, and cough for one week. He had had milder attacks of a similar nature, consisting of dyspnea, rapid pulse, and edema for five years. On physical examination the patient was restless and slightly orthopneic, with a respiratory rate of 40 per minute. There was ashen cyanosis of the lips and the nail beds, marked pallor of the face and extremities, and profuse sweating. The veins of the neck appeared distended, but the superficial veins of the extremities were completely collapsed and would not fill when occluded above. The heart was enlarged, rate 150, but no significant murmurs were heard. The blood pressure could not be obtained by the auscultatory method, apparently because of the minute pulse pressure. Palpation of the barely perceptible pulse at the wrist, however, demonstrated the systolic pressure to be about 120 mm. Hg. The lungs were filled with râles, and there was pitting edema up to the hips.

The pressure in the cubital vein could not be obtained because the superficial veins were bloodless, but the pressure in the femoral vein was 41 cm. of water. In addition to having severe circulatory collapse as evidenced by pallor, sweating, restlessness, and weak pulse, there was advanced congestive failure. The almost complete absence of blood flow to the skin and extremities, which is so frequently the case in collapse, plus the inability of the blood in the superficial veins to flow backward past the valves, probably accounts for the absence of blood in these veins. In such instances, the central venous pressure can be obtained only in a large vein, such as the femoral, which communicates directly with the right auricle without intervention of valves.

CASE 11.—M. R., a twenty-nine-year-old woman, entered the Boston City Hospital complaining of profound muscular weakness, a red scaly rash over the face and knuckles for eight months, and generalized edema for four months. She was studied extensively and diagnosed dermatomyositis by Dr. J. C. Turner, who will report the case in full.[10] Because of the marked generalized brawny edema, puncture of superficial arm or leg veins was practically impossible. The femoral vein was penetrated easily, and the pressure found to be 10 cm. of water. At the same time blood was removed for chemical analysis. The femoral venepuncture in this case not only ruled out cardiac failure as a factor in her edema, but also furnished blood for diagnostic study.

DISCUSSION

The simplicity and the accuracy of direct determination of the venous pressure in the larger veins make it a valuable diagnostic aid in any case in which there is a question of a circulatory disorder. In many instances careful observation of the superficial veins will give a fairly accurate estimation of the pressure in these veins. However, this method cannot be applied to the veins of the legs with any degree of accuracy, or even to the veins of the arms, in the presence of a very high venous pressure, venous thrombosis, edema, or obesity. A knowledge of the pressure in both cubital veins enables one to detect an obstruction in either of the subclavian or innominate veins. Since normally the pressure on the two sides is the same, any difference indicates an obstruction, and the amount of the difference gives an

estimate of the degree of obstruction. Likewise a knowledge of the pressure in both the cubital and the femoral veins enables one to determine the location and degree of an obstruction in either the superior or inferior vena cava, or both.

The femoral vein, because of its constant position, its large size, and the absence of valves between it and the heart, offers at times the only practical site for the determination of systemic venous pressure or for the removal of blood. Leading as it does directly into the inferior vena cava, which in turn leads directly into the right auricle, the femoral vein is always well filled with blood under at least the same pressure as in the right auricle. Abnormal variations of pressure in the auricle such as occur with tricuspid regurgitation are freely transmitted to the femoral vein without interference from values. A knowledge of the pressure in the right auricle is essential in order to estimate the functional state of the heart and the peripheral circulation. When the pressures are determined simultaneously in both the cubital and the femoral veins, the significance of the measurements is increased, not only in relation to the general circulation but also in relation to local obstructive lesions which interfere with venous flow.

SUMMARY

1. A knowledge of the pressures obtained simultaneously in the veins of the arms and legs is of clinical significance. Cases are reported which illustrate the value of comparative measurements of the pressure in the cubital and femoral veins.

2. The femoral vein may be advantageously utilized not only for measuring the venous pressure but also for obtaining blood and for administering intravenous medication.

REFERENCES

1. Overholt, R. H., and Pilcher, L. S., Jr.: Changes in Venous Pressure After Thoracoplasty—Its Significance in Relation to the Extent of Rib Removal, J. Thoracic Surg. **4**: 269, 1935.
2. Villaret, M., and Desoille, H.: Quelques examples cliniques montrant l'intérêt général de la phlébopiézométrie au point de vue du diagnostic, du prognostic, et de la thérapeutique, Presse méd. **40**: 1477, 1932.
3. Griffith, G. C., Chamberlain, C. T., and Kitchell, J. R., Jr.: Observations on the Practical Significance of Venous Pressure in Health and Disease, With a Review of the Literature, Am. J. M. Sc. **187**: 642, 1934.
4. Brams, W. A., Katz, L. N., and Kohn, L.: The Effect of Abdominal Distention and Release on the Blood Pressures in the Arteries and Veins, Am. J. Physiol. **104**: 120, 1933.
5. Weiss, Soma, and Ellis, Laurence B.: The Circulatory Mechanism and Unilateral Edema in Cerebral Hemiplegia, J. Clin. Investigation **9**: 17, 1930.
6. Florkin, M., Edwards, H. T., and Dill, D. B.: Oxygen Utilization in the Legs of Normal Men, Am. J. Physiol. **94**: 459, 1930.
7. Harrison, T. R., and Pilcher, C.: Studies in Congestive Failure: I. The Effect of Edema on Oxygen Utilization, J. Clin. Investigation **8**: 259, 1930.
8. Moritz, F., and von Tabora, D.: Ueber eine Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu bestimmen, Deutsches Arch. f. klin. Med. **98**: 475, 1910.
9. Weiss, Soma, and Wilkins, Robert W.: The Nature of the Cardio-Vascular Disturbances in Vitamin Deficiency States, Tr. A. Am. Physicians **51**: 341, 1936.
10. Turner, Joseph C.: Dermatomyositis: Unpublished Studies.

THE VALUE OF DIRECT VENOUS PRESSURE ESTIMATIONS IN AMBULATORY CARDIAC PATIENTS*

A. R. Berger, M.D.
New York, N. Y.

WELL-DEFINED congestive heart failure presents a clinical picture which is unmistakable. Preceding this state, patients usually have subjective evidence of diminished cardiac reserve—namely, dyspnea on effort and abnormal fatigue. Such symptoms, however, by their very nature are notoriously unreliable. They are exaggerated by the neurotic and apprehensive, and minimized by the stolid and phlegmatic types of patients. They may be caused by many conditions wholly unrelated to cardiac insufficiency.

Detection of the earliest objective signs of heart failure—if possible before subjective symptoms are particularly noticeable—is of extreme value in the management of ambulatory cardiac patients. The patient's habits of living, or his medication, may be rearranged, or any other necessary therapy may be introduced to prevent, if possible, the development of failure. A search for objective phenomena includes the application of the following methods of approach: response to effort; determination of cardiac output, venous pressure, and vital capacity.

Various procedures have been devised to increase the work of the patient in a standard manner in order to detect objective evidence of heart failure.[1-5] The criteria usually employed are the blood pressure and the heart rate. However, the complex phases of metabolism in muscular exercise and the effect of training come into operation. It is readily apparent that these tests merely record the efficiency of the vasomotor control of circulation and that they do not indicate true cardiac efficiency. Respiratory tests[6-8] are subject to similar criticism, and additional complications exist in the form of diseases of the lungs, pleura, mediastinum, or of the respiratory musculature. In both types of tests, neurogenic or psychogenic factors (fear and apprehension), and deliberate malingering are potent sources of error.

Although the heart has long been compared to a pump, it is extremely difficult to determine the efficiency of this biological machine by means of cardiac output. It is not possible to make direct observations in man without a certain amount of hazard. Ever since the work of Fick in 1870, interest has been stimulated in the gasometric determi-

*From the Department of Medicine and Therapeutics, New York University College of Medicine, the Third (New York University) Medical Division of Bellevue Hospital, and the Cardiac Clinic of Bellevue Hospital.

nation of cardiac output. The original method and its subsequent modifications are rather complicated and require a highly specialized technic. Inadequate mixture in the lung-bag system and failure to obtain equilibrium between the gases in the alveolar air and those in the blood introduce errors. As Grollman[9] has pointed out, there are inaccuracies in determinations in normal subjects, and there may be an elevation of even 25 per cent because of psychic disturbances. The only advantage which the indirect method recently described by Bazett[10] has over the respiratory method is its applicability to very ill persons.

Physiological study has shown that within certain limits increasing the initial tension on skeletal muscle during contraction increases its work done. Patterson and Starling[11] and Straub[12] have demonstrated the same facts for cardiac muscle. The initial load in the ventricle just prior to systole is the pressure of the blood within it. This is determined by filling from the auricle, which, in turn, is modified by venous return and venous pressure. Hence, the peripheral venous pressure bears a linear relationship to the initial intraventricular pressure.

If the "backward-failure" hypothesis of Hope (the evidence for which is considered comprehensively by Harrison[13]) is accepted, the measurement of venous pressure, on theoretical grounds, should prove the best objective evidence of early failure. As stated by Eyster,[14] "careful and frequent determinations of venous pressure show that the changes in pressure in many cases precede the changes in symptoms and signs, and may thus serve as an indicator of impending change." In the case of the right ventricle it is simple to measure the venous pressure. The venous pressure in the pulmonary circulation, which conditions the initial left intraventricular pressure, cannot, however, be determined in man. For this reason, the vital capacity may be studied to detect early left ventricular failure.

It was hoped that these two objective signs—peripheral venous pressure and vital capacity—might furnish early evidence of failure so that treatment could be instituted promptly before clinical failure developed. With this in mind, the following study was undertaken.

MATERIAL

The results embodied in this paper were obtained from an intensive study (over a period of four years) of 68 male patients in the adult cardiac clinic of Bellevue Hospital. The distribution according to etiology and rhythm is shown in Table I.

The rheumatic group includes those patients without any history of the manifestations of rheumatic fever but in whom, nevertheless, the typical structural changes of rheumatic heart disease are found. In

TABLE I

RHEUMATIC (AND UNKNOWN-RHEUMATIC TYPE)		ARTERIOSCLEROSIS AND HYPERTENSION		ARTERIOSCLEROSIS AND UNKNOWN (PREVIOUS HYPERTENSION)		RHEUMATIC HYPERTENSION —ARTERIO-SCLEROSIS		HYPERTENSION AND UNKNOWN (RHEUMATIC)		ARTERIO-SCLEROSIS		HYPER-THYROID		UNKNOWN	
RSR*	AF†	RSR	AF	RSR	AF	RSR	AF	RSR	AF	RSR	AF	RSR	AF	RSR	AF
2	27	5	8	2	9	-	2	2	-	2	-	1	-	2	6

*Sinus rhythm.
†Auricular fibrillation.

the group designated "arteriosclerosis and unknown," the unknown factor is most probably an antecedent hypertension. The "hypertension—unknown (rheumatic)" group includes two patients who have mitral stenosis and insufficiency so that the unknown factor here is considered to be rheumatic fever. The "unknown" group comprises patients with organic heart disease without any definitely ascribable etiology. The other group labels are self-explanatory. All the patients with the rheumatic type of heart disease, thirty-three in number, have mitral stenosis and insufficiency, and nine also have aortic valve disease (seven with aortic insufficiency and two with aortic insufficiency and aortic stenosis). The diagnoses of tricuspid or pulmonic disease, or adherent pericardium, were not made clinically, nor were they encountered in the cases which came to necropsy. The ages range from twenty-two to seventy-nine years.

The control group includes twenty male patients convalescent from minor ailments. They are selected only so far as they show no evidence of organic heart disease and they parallel the age group of the patients' series.

METHOD

The method* is a modification of the one described by Moritz and von Tabora.[15] The apparatus consists of a manometer capable of being adjusted so that its zero reading is in the same horizontal plane as the right auricle. In the recumbent position, the level of the right auricle is considered to be in the fourth intercostal space, 5 cm. below the sternum. A three-way stopcock connected to a syringe and to the manometer insures proper cannulation before the manometer is put into communication with the vein. The system contains a sterile 5 per cent sodium citrate solution and the needle is 1 inch long and of 18 gauge caliber. The vein usually used is the median basilic or a major tributary. All constricting upper garments are removed. A basal rest period of at least fifteen minutes, in which the patient remains absolutely quiet, flat on his back, precedes the test. All readings are checked, and a Valsalva experiment is performed each time. Heart rate and respirations are recorded at the same time and vital capacity is determined the same evening. The patients complained of no discomfort when the operator was sufficiently skillful.

*Before undertaking this investigation, Dr. Erna Enderle and Dr. M. S. White made a preliminary survey of the relative ease and merits of the indirect and direct methods of venous pressure determination. One hundred unselected patients, representing the population of a general medical service, male and female, young and old, cardiac and noncardiac, were studied. Following a basal rest period of fifteen minutes, during which it was noted that no marked variation occurred in heart and respiratory rates, venous pressure was determined first by the Eyster method, and then immediately afterward by the modified Moritz—von Tabora method. In 32 patients, no suitable (visible) vein could be found. Of the remaining 68 cases, venous pressures could be obtained by the indirect method in only 51 because of various difficulties with the apparatus. A reading was obtained by the direct method in all 100 patients. In none of the 51 cases with indirect and direct pressure readings was any exact coincidence noted. Because of its ease, accuracy and reliability, the direct method was selected for use in the present study.

TABLE II

		CONTROL	RHEUM.		AS.-HYP.		AS.-UNK.		RH. HYP. AS	HYP. UNK.	AS.	HY-PERTH.	UNK.	UNK.
			AF	RSR	AF	RSR	AF	RSR	AF	RSR	RSR	RSR	AF*	RSR
NO. OF CASES		20	27	2	8	5	9	2	2	2	2	1	6	2
AV. FOR GROUP		7.7	9.4	6.8	7.5	4.6	7.2	4.0	10.7	5.9	7.0	4.7	8.8	4.4
Range between min. and max.	0- 2.9	15	3	1	1	3	2	1	–	–	–	–	–	1
	3- 5.9	4	11	–	3	1	3	1	1	2	–	1	4	–
	6- 8.9	1	5	–	4	1	2	–	1	–	1	–	2	1
	9-11.9	–	6	1	–	–	1	–	–	–	1	–	–	–
	12-14.9	–	–	–	–	–	1	–	–	–	–	–	–	–
	15-17.9	–	2	–	–	–	–	–	–	–	–	–	–	–

*Includes one case of auricular flutter.

RESULTS

The results obtained from the study of a group of 20 normal individuals are summarized in the first column of Table II. These observations were made at about the same time each day under the same controlled conditions, namely, rest period of fifteen minutes, and heart and respiratory rates showing only very slight fluctuation. Fifteen cases show a range of 2.9 cm. or less between minimum and maximum;

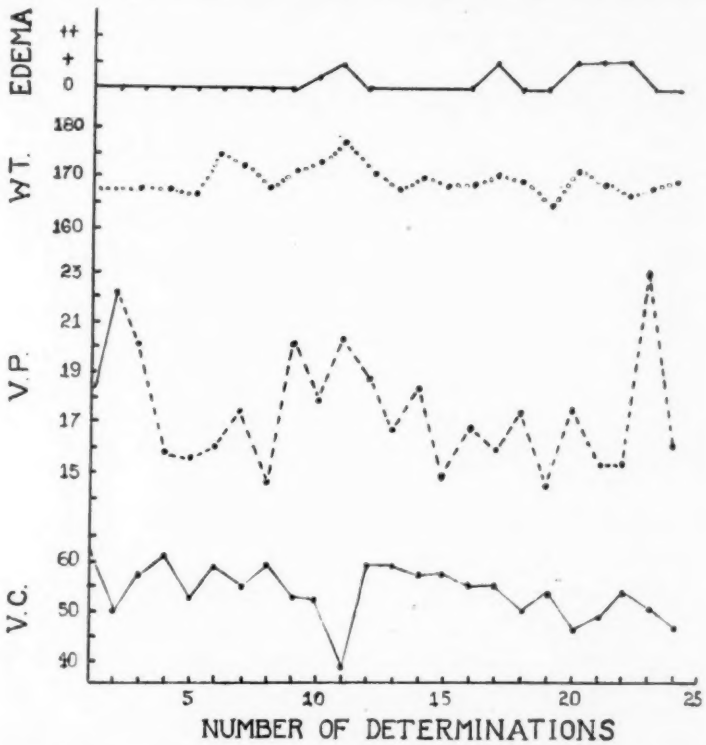

Fig. 1.—Typical case of rheumatic heart disease, with mitral stenosis and insufficiency and auricular fibrillation. Vital capacity (*V.C.*) in percentage of normal (according to the Peabody scale), venous pressure (*V.P.*) in centimeters of water, weight (*Wt.*) in pounds, and the degree of peripheral edema are plotted for each clinic visit.

14 cases range from 3 to 5.9 cm.; and one case ranges between 6 and 8.9 cm. Case 19 shows the fluctuation over a nineteen-minute interval of continuous observation. Cases 21, 22, and 23 illustrate the changes

CASE 19	CASE 21	CASE 22	CASE 23
6:20 9.4	10:30 A.M. 8.5	10:30 A.M. 4.0	4:15 4.2
6:22 8.3	11:30 A.M. 9.0	11:00 A.M. 4.1	4:45 4.1
6:25 6.5	meal	meal	meal
6:27 7.4	12:15 P.M. 6.2	2:45 P.M. 2.2	5:30 3.6
6:28 7.2	12:45 P.M. 6.0	4:00 P.M. 2.2	5.45 3.4
6:29 6.7	4:00 P.M. 8.4	4:30 P.M. 3.0	6:15 4.3
6:30 6.0		5:00 P.M. 4.4	
6:33 6.1			
6:36 6.2			
6:39 6.3			

during the day and also suggest that meals may influence venous pressure, contrary to the statement of Eyster.[14]

The remaining columns of Table II summarize the results of the study of 68 patients. They are tabulated according to etiology and rhythm. Although the group as a whole has well-advanced heart disease, a reading is not included if the patient was considered clinically to be in congestive failure at the time the determination was made. All the patients are well digitalized and the factor of heart rate is controlled. The respiratory rate did not show any significant change.

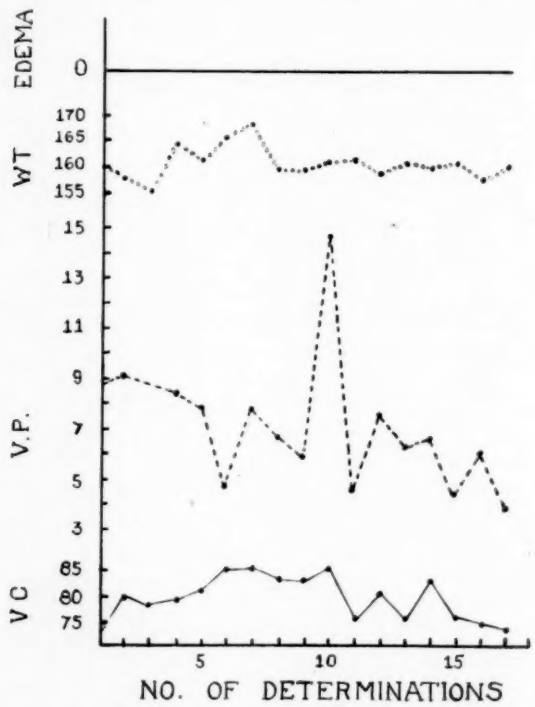

Fig. 2.—Typical case of hypertensive-arteriosclerotic heart disease with auricular fibrillation.

The average venous pressure for the group as a whole is essentially the same as in the control group—7.6 cm. for the cardiac patients against 7.7 for the normal subjects. The fluctuation between minimum and maximum is greater than in the normal series. Within the series, the rheumatic-hypertension-arteriosclerosis group has the highest level of venous pressure (10.7 cm.). The numerically largest group (rheumatic with 29 cases) has the next highest level (9.2 cm.), and this is above the normal group value.

Figures 1 and 2 are taken from two typical cases. Vital capacity, weight, edema, and venous pressure are plotted for each visit. These

cases illustrate a finding noted on several occasions, namely, an inexplicable rise in venous pressure, unassociated with any change in the patient's immediate condition or in his subsequent course.

The effect of cardiac rate and rhythm on venous pressure when these factors produce congestive symptoms has long been appreciated.[14] Fig. 3, taken from the case of auricular flutter, illustrates the effect of carotid sinus pressure. The ventricular rate was reduced from 120 to 60 and the venous pressure dropped from 10.6 cm. to 4 cm. This observation was repeated once at a later date.

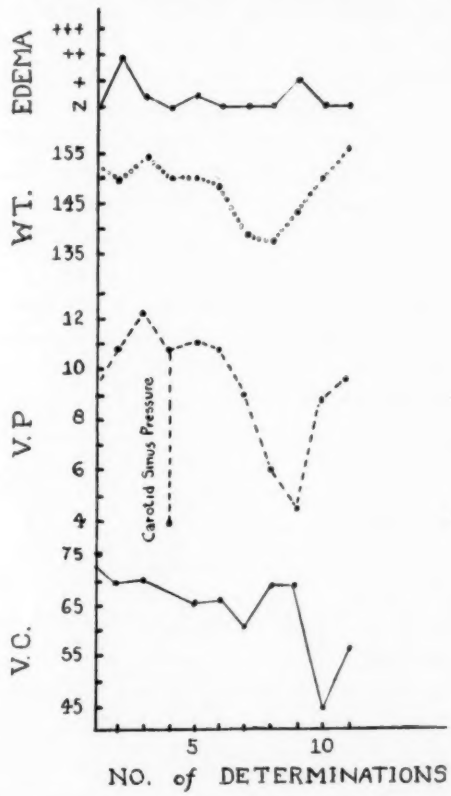

Fig. 3.—Case of auricular flutter of ten years' duration. The effect of carotid sinus stimulation on venous pressure is shown.

Although patients showed sporadic elevation of venous pressure without congestive failure, there was a distinct correlation between a sustained rising venous pressure and the appearance of failure, as noted by Eyster. However, the usual clinical signs were apparent at the same time that the pressure first became elevated. Case 71 had clinical evidence of well-defined failure with a pressure of 8.1 cm. On at least ten other occasions, his pressure was over this value, ranging up to 11.0 cm. Thus, this case might be considered to be one of failure in the absence of any marked elevation of venous pressure.

In Case 45 the patient was in congestive failure on Feb. 23, 1933, with a pressure of 13.7, yet on Aug. 24, 1933, with a pressure of 13.6, he apparently was entirely free from clinical symptoms.

There were four cases in which negative venous pressures were obtained, three in the arteriosclerosis and hypertension group, and one in the arteriosclerosis and unknown group.

DISCUSSION

A critical evaluation of the significance of changes in venous pressure in ambulatory cardiacs must include answers to these questions: 1. What is the normal range and variation in venous pressure? 2. Can venous pressure become elevated above normal without other signs of failure being present? 3. Is a rise in venous pressure the earliest or the most reliable sign of failure?

In the normal group the average venous pressure did not exceed 10.4 cm. although a maximum of 13.3 was obtained. This average figure is in accord with the normals quoted by Eyster.[14] Hooker and Eyster,[16] with indirect measurements, found that "a variation between a few centimeters of positive pressure up to 18 cm. is not uncommon, and the range of pressures was large" in a normal group. Bedford and Wright[17] also reported a considerable normal variation, using the direct method. Inasmuch as both the direct and indirect methods have been employed, any implication that variation is due to the direct determination is not justifiable. If normal venous pressure is subject to such fluctuation, its significance in determining an abnormal state is automatically lessened.

The answer to the second question calls for a consideration of the sporadic marked elevations in pressure referred to previously. No satisfactory explanation could be found at the time of the observation on the basis of physical findings or even in subjective complaints. The subsequent course during the next few months likewise failed to give any clue to the rise. Local causes and technical errors excluded, one can only conjecture at some mechanism which produces a temporary venous hypertension.

The exact nature of this mechanism is not clear. Henderson and his associates[18] have demonstrated variations in intramuscular tonus and found that this tonic intramuscular pressure is of extreme importance in the venous return to the heart. Widespread variation in muscle tonus, affecting venous return and pressure, may be the underlying cause for the fluctuations noted. Another theoretical explanation is that of venous spasm, a mechanism analagous to that invoked for arteries in many cases of transient arterial hypertension. The occurrence of venous spasm is supported by the clinical experience in which a vein contracts rapidly when a venipuncture is attempted.*

*This has been seen by Evans: New England J. Med. 207: 934, 1932.

In this series, a sustained rise in venous pressure could not be demonstrated in any case at an appreciable interval before clinical signs of failure developed. To be sure, a rise roughly paralleled the appearance of failure, but venous pressure itself could not be used in the long-range prognostication of impending failure. Therefore, unless one is aware of the fact that sporadic marked elevations of pressure can occur, finding such an elevation on a single occasion might lead to the erroneous conclusion that failure is impending. The evidence gathered in this study indicates that, although venous pressure rises with the appearance of congestive heart failure, it is not the most reliable, nor necessarily the earliest, sign of failure.

SUMMARY

A brief summary of the methods in use for studying circulatory efficiency is given and the physiological rationale of venous pressure determinations is discussed.

The results of an intensive study of 68 ambulatory cardiac patients are analyzed and compared with a control series. The average venous pressure for the cardiac group as a whole is the same as for the control group, although the former shows a greater fluctuation. Rise in venous pressure roughly parallels the development of congestive heart failure but it does not antedate the appearance of clinical symptoms.

The author wishes to thank Dr. Arthur C. DeGraff for his helpful suggestions throughout the course of this investigation.

REFERENCES

1. Brittingham, H. H., and White, P. D.: Cardiac Functional Tests, J. A. M. A. **79**: 1901, 1922.
2. Gillespie, R. D., Gilson, C. R., and Murray, D. S.: Effect of Exercise on Pulse Rate and Blood Pressure, Arch. Int. Med. **12**: 1, 1925.
3. Schneider, E. C.: A Cardiovascular Rating as a Measure of Physical Fatigue and Efficiency, J. A. M. A. **74**: 1507, 1920.
4. Schmitz, H. W.: Vital Capacity, Respiratory Frequency, Pulse Rate and Systolic Blood Pressure in Heart Disease: Their Importance in Classifying Patients, Arch. Int. Med. **36**: 628, 1925.
5. Master, A. M.: The Two-Step Test of Myocardial Function, Am. Heart J. **10**: 495, 1935.
6. Peabody, F. W., and Sturgis, C. C.: Clinical Studies in Respiration. VII. Effect of General Weakness and Fatigue on the Vital Capacity of the Lungs, Arch. Int. Med. **28**: 501, 1921.
7. Peabody, F. W., and Sturgis, C. C.: Clinical Studies in Respiration. IX. Effect of Exercise on the Metabolism, Heart Rate and Pulmonary Ventilation of Normal Subjects and Patients With Heart Disease, Arch. Int. Med. **29**: 277, 1922.
8. Peabody, F. W., and Wentworth, J. A.: Clinical Studies in Respiration. V. Vital Capacity of the Lungs and Its Relation to Dyspnea, Arch. Int. Med. **20**: 443, 1917.
9. Grollman, A.: Cardiac Output in Health and Disease, Baltimore, 1932, Charles C. Thomas.
10. Bazett, H. C., Cotton, F. C., Laplace, L. B., and Scott, J. C.: The Calculation of Cardiac Output and Effective Peripheral Resistance From Blood Pressure Measurements, With an Appendix on the Size of the Aorta in Man, Am. J. Physiol. **113**: 322, 1935.

11. Patterson, S. W., and Starling, E. H.: On the Mechanical Factors Which Determine the Output of the Ventricles, J. Physiol. **48:** 357, 1914.
12. Straub, H.: Dynamik des Säugetierherzens, Deutsches Arch. f. klin. Med. **115:** 531, 1914.
13. Harrison, T. R.: Failure of the Circulation, Baltimore, 1935, Williams & Wilkins Company.
14. Eyster, J. A. E.: The Clinical Aspects of Venous Pressure, New York, 1929, Macmillan Company.
15. Moritz and von Tabora: Über ein Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu bestimmen, Deutsches Arch. f. klin. Med. **98:** 475, 1910.
16. Hooker, D. R., and Eyster, J. A. E.: An Instrument for the Determination of Venous Pressure in Man, Bull. Johns Hopkins Hosp. **19:** 274, 1908.
17. Bedford, D. E., and Wright, S.: Observations on Venous Pressure in Normal Individuals, Lancet **2:** 106, 1924.
18. Henderson, Yandell, Oughterson, A. W., Greenberg, L. A., and Searle, C. P.: Muscle Tonus, Intramuscular Pressure and the Venopressor Mechanism, Am. J. Physiol. **114:** 261, 1936.

THE TRANSITIONS BETWEEN NORMAL SINUS RHYTHM, VENTRICULAR ESCAPE, A-V NODAL RHYTHM, AND A-V DISSOCIATION

A Report of 12 Cases, Including 7 Showing Interference Dissociation*

Frank B. Cutts, M.D.
Providence, R. I.

DURING the past two years there have appeared at this hospital five patients whose electrocardiograms have shown the control of the ventricular beat changing frequently between the sino-auricular node and the auriculoventricular node. Interest in these cases stimulated a search through the electrocardiographic files, which contain tracings on somewhat over 8,000 patients, and seven additional cases were discovered exhibiting this same unusual condition. As previous reports in the literature on this subject have been based, in most instances, on study of two or three patients, it was felt that a group of cases of even this modest size might yield some information of interest.

It is worthy of emphasis that in the electrocardiograms in this series the control of the ventricular beat vacillated almost continuously between the sino-auricular and the auriculoventricular nodes—the disturbance in rhythm being usually discernible in all the three conventional leads. Therefore, the following types of related rhythm abnormality are not considered here: (1) Tracings in which the P-wave changes in form or amplitude but maintains its normal position in front of the QRS complexes. Such changes are believed to be due to the displacement of the site of impulse formation from the more irritable upper to the less irritable lower portions of the sino-auricular node, resulting perhaps from variations in vagal tone.[1, 2] (2) Instances of complete heart-block. (3) Instances of isolated or relatively infrequent ventricular escape. This exclusion of transient ventricular escape is admittedly arbitrary, for the same factors that produce ventricular escape will, if they become more pronounced, result in persistent interference dissociation or A-V rhythm.[3] However, transient ventricular escape is relatively common and well understood, while the types of irregularity under discussion here are rather rare.

It will be well at this point to indicate what we mean by A-V rhythm, A-V dissociation, and interference dissociation, and to outline the conditions under which these abnormalities in rhythm may appear. A-V

*From the Heart Station of the Rhode Island Hospital, Providence, R. I., under the direction of Dr. Frank T. Fulton.

rhythm occurs when the entire heart, both auricles and ventricles, responds to impulses arising in the A-V node. Under such conditions the A-V node is more irritable than the S-A node, thereby discharging impulses at a more rapid rate. The QRS complexes are usually similar, except for minor variations, to those occurring when the heart responds to impulses of sino-auricular origin. The P-waves are usually inverted (indicating retrograde conduction) and may appear shortly before, during, or after the QRS complexes. In a few instances, however, the P-waves may be upright in lead I.[4, 5] A-V dissociation occurs when the auricles and ventricles are beating independently, the auricles responding to the S-A node and the ventricles to the A-V node. When both forward and retrograde conduction between the auricles and ventricles are blocked, at a slow heart rate, the common type of complete heart-block results. When, however, as occurs in seven of the cases under discussion here, (1) only retrograde conduction is blocked and (2) the A-V node is more irritable and is discharging impulses at a faster rate than the S-A node; the ventricles respond part of the time to the A-V node and part of the time to the S-A node, the latter occurring when impulses from this node fall at a time when the ventricles are no longer refractory as a result of the previous contraction. Because of the retrograde conduction block, the auricles respond only to the slower S-A node. Thus beats of S-A origin are interspersed in a record that otherwise has the appearance of complete A-V dissociation. This interplay between the S-A and the A-V nodes, with the resulting ventricular irregularity, is an example of interference dissociation.[6] In this condition the P-waves are upright (except perhaps in Lead III),[7] and they characteristically do not have any constant time relation with the QRS complexes.[8]

In order for the transitions between normal sinus rhythm, ventricular escape, A-V rhythm, and A-V dissociation to occur, it is usually necessary for the S-A and the A-V nodes to have, temporarily at least, nearly the same rate of impulse formation. Under such conditions a relatively slight change in the rhythm of one node or the other, due to variation in vagal or sympathetic tone or some other cause, may cause a transition to some other type of rhythm. In one case observed by Jones and White,[9] a change from the recumbent to the sitting position was frequently followed by a change from S-A to A-V rhythm.

There are three conditions under which the A-V node may become more irritable than the S-A node and hence initiate a change from normal sinus rhythm to ventricular escape, A-V rhythm, or A-V dissociation:[10] (1) When there is considerable depression of the S-A node. Such a condition is often associated with marked sinus arrhythmia and may arise as a result of deep respiration,[11] pressure on a sensitive carotid sinus,[10] digitalis[10, 12] or quinidine[13] administration, ocular pressure,[14] or some ill-defined or unknown cause. It has been shown to be associ-

ated at times with the partial asphyxia occurring with Cheyne-Stokes respiration.[15] (2) When there is increased irritability of the A-V node. This may result from infection,[16] especially rheumatic infection,[8] from administration of atropine,[10] especially in the first few minutes of its effect,[12, 14, 17] or again from unknown causes. (3) When there is a combination of the two effects described in 1 and 2.[10] In experimental animals the A-V node may become more irritable than the S-A node as a result of (a) destruction of the S-A node, (b) cooling the S-A node, (c) warming the A-V node, or (d) stimulation of the right vagus and the left sympathetic nerves.[18]

Following are brief summaries of the hospital records of a few representative cases. For the most part only the cardiac symptoms and signs are recorded here.

CASE 1.—(Case 9 in Table I.) B. F., thirty-seven-year-old white, single, French knitter, was admitted Nov. 19, 1934, complaining of weakness for several years and a slow heart rate for an unknown period. The past history was irrelevant. Fifteen and seven years previously she had "nervous breakdowns," the nature of which she could not explain adequately. Six years ago she noticed the onset of a head tremor, which has persisted to date. Four weeks prior to entry she had the grip and since that time had been conscious of a slow forceful heart action and increased weakness.

The significant findings on physical examination were the presence of a constant fine tremor of her head and the cardiac abnormality. On November 21 the following was noted: The heart appeared slightly enlarged to percussion. The rate was 48 per minute, and the rhythm was not completely regular, as the heart was observed to speed up for a few beats about every 20 seconds. There were no definite murmurs, but the heart sounds were not always the same—at times the first and second sounds were loud and clear, while at other times both sounds seemed slurred and reduplicated. Occasional vigorous pulsations were observed in the neck veins, occurring after the first sound was heard at the apex. On November 27 the patient was fluoroscoped, and an orthodiagram was made. The heart diameter was 11.8 cm. and the chest diameter was 20.5 cm. No definite enlargement of any heart chamber was detected. The cardiac pulsations were very vigorous and at times the auricles could be seen to beat after the beginning of the ventricular contractions. This was best seen in the right oblique view.

Laboratory studies, except electrocardiography, contributed no positive information. The Wassermann reaction was negative; the urine and blood were normal; and the blood urea nitrogen and the blood sugar were within normal limits.

She gradually improved without medication and was discharged Dec. 8, 1934. When last seen, May 4, 1935, she was feeling well and had no complaints.

Electrocardiographic Findings.—The same type of arrhythmia present in Fig. 1 was also present in Cases 1, 4, 7, and 10 (Table I). In order to conserve space, and since little or no information would be added by their detailed presentation, Fig. 1 is considered illustrative of the irregularities of rhythm in these five cases.

It is readily seen that the fundamental abnormality in this record is a change from S-A rhythm to A-V rhythm, and then back again to S-A rhythm. An important predisposing factor in this change is the

presence of marked sinus arrhythmia, the interval between auricular beats varying from 0.92 sec. to 1.60 sec. (the interval between auricular beats 10 and 11 and between 2 and 3). When the auricular rate slows up sufficiently, the A-V node escapes and takes control of the ventricular beat. This is seen to occur at beat 3. Auricular beat 3 is apparently buried within the QRS complex. Auricular beat 4 is of some interest as a transitional beat. The P-wave is nearly isoelectric. This is probably due to the fact that impulses from the S-A and the A-V nodes have reached the auricles at about the same instant so that a portion of the auricles responds to each center. This is the explanation offered by Lewis[18] for similar auricular waves.

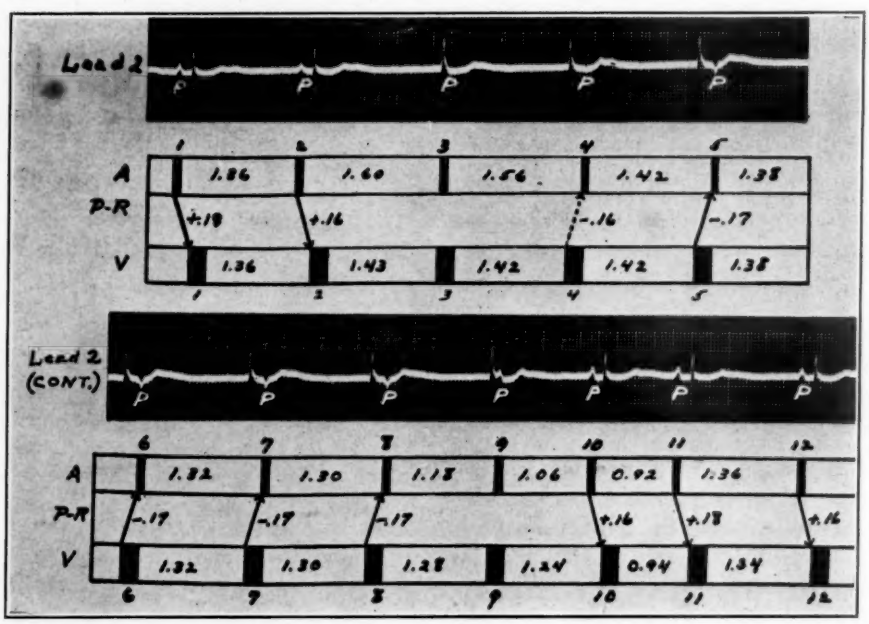

Fig. 1.—B. F. Continuous tracing in Lead II, Nov. 20, 1934. The diagrams beneath this and the subsequent electrocardiograms are arranged in identical fashion and may be described together. The vertical black bars in the upper strip marked *A* represent the auricular beats and are placed directly beneath the P-waves in the accompanying electrocardiogram. The interval between the auricular beats is recorded in hundredths of a second. In the middle strip, marked *P-R*, are recorded in hundredths of a second the P-R intervals (preceded by a plus sign) or the R-P intervals (preceded by a minus sign)—depending on whether conduction is from auricles to ventricles or vice versa. The arrows in this middle strip indicate the direction of impulse conduction and are included only when it seems probable that a beat has been actually conducted. In the bottom strip, marked V, the heavy vertical bars represent and are placed directly beneath the ventricular beats. The interval between beats is recorded in hundredths of a second. The auricular and ventricular beats are numbered consecutively in each diagram. Note especially the variation in the form and position of the P-waves.

By beat 5, A-V nodal rhythm is fully established, and there is undisturbed retrograde conduction from ventricles to auricles. Finally at auricular beat 9, the S-A node has discharged an impulse before one has been conducted from the A-V node, and thus the S-A node takes

control of the auricle, causing an upright P-wave. By auricular beat 10, the S-A node has speeded up sufficiently to regain control of the entire heart.

During the period when the ventricles are under the control of the A-V node (beats 3 through 9), it is to be noted that there is some irregularity, the interventricular intervals varying from 1.43 sec. to 1.28 sec., but this arrhythmia is much less pronounced than is the sinus arrhythmia. The QRS complexes are nearly the same regardless of which node is in control. Ventricular beat 3 shows a higher R-wave because of the simultaneous occurrence of R-wave and upright P-wave. Slurring occurs slightly higher on the descending limb of the R-wave when the beats are of A-V nodal origin (e.g., ventricular beats 7 and 8) than when they are of S-A origin (e.g., beats 1 and 2). The R-P interval (0.17 sec.) is practically identical with the P-R interval (0.16-0.18 sec.).

After the control tracing reproduced above was taken, the effect of various other procedures on the rhythm was tried. Right and left carotid sinus pressure for a period of forty seconds produced no detectable changes in the electrocardiogram. A drink of iced water was without effect. The patient rapidly raised her trunk to assume the sitting position twenty times with resulting mild dyspnea, and yet the arrhythmia portrayed above persisted. However, the ventricular rate remained at 46, as in the control tracing, and it is quite possible that more intensive exercise or the administration of adrenalin might have yielded different results. Finally 1/37 gr. (4 tablets of 1/150) of atropine was given subcutaneously. After fifteen minutes the rhythm was much more regular, mostly S-A in origin, but a few A-V nodal beats persisted, the ventricular rate at this time being 76. After thirty minutes the first half of the tracing showed beats of S-A origin, but this then changed to A-V nodal rhythm (rate 56). The most striking change following atropine administration was the disappearance of the gross irregularity in rhythm. The dose of atropine was perhaps not large enough for full atropinization, and the tracings should have been taken more frequently. However, the appearance of A-V nodal beats at a rate of 76 per minute does indicate that at that time the A-V node was released from vagal control[17] or stimulated[18] fully as much by the atropine as was the S-A node.

A tracing was finally made May 4, 1935, some six months after that shown in Fig. 1, and at that time all the beats were of S-A origin though a moderate degree of sinus arrhythmia persisted.

CASE 2.—(Case 12 in Table I.) F. J., sixty-nine-year-old white, married, Roumanian housewife, was admitted on Dec. 21, 1931, with the symptoms and signs of bronchopneumonia. She had been very obese—weight 275 pounds, height 5 feet 2 inches—for years and had become progressively dyspneic over the same period.

The outstanding findings on physical examination were the marked obesity, scattered râles through both chests, and a blood pressure of 230/130. Examination of the heart was unreliable because of the immense fat pads. During the first half of her hospital stay she ran a fever up to 101° F., but she slowly improved and left for a bed-and-chair existence at home on March 9, 1932.

She remained a cardiac invalid and could not take more than a few steps without experiencing dyspnea. She finally died at home in October, 1932. The details of her death are not known, but she apparently suffered from progressive heart failure.

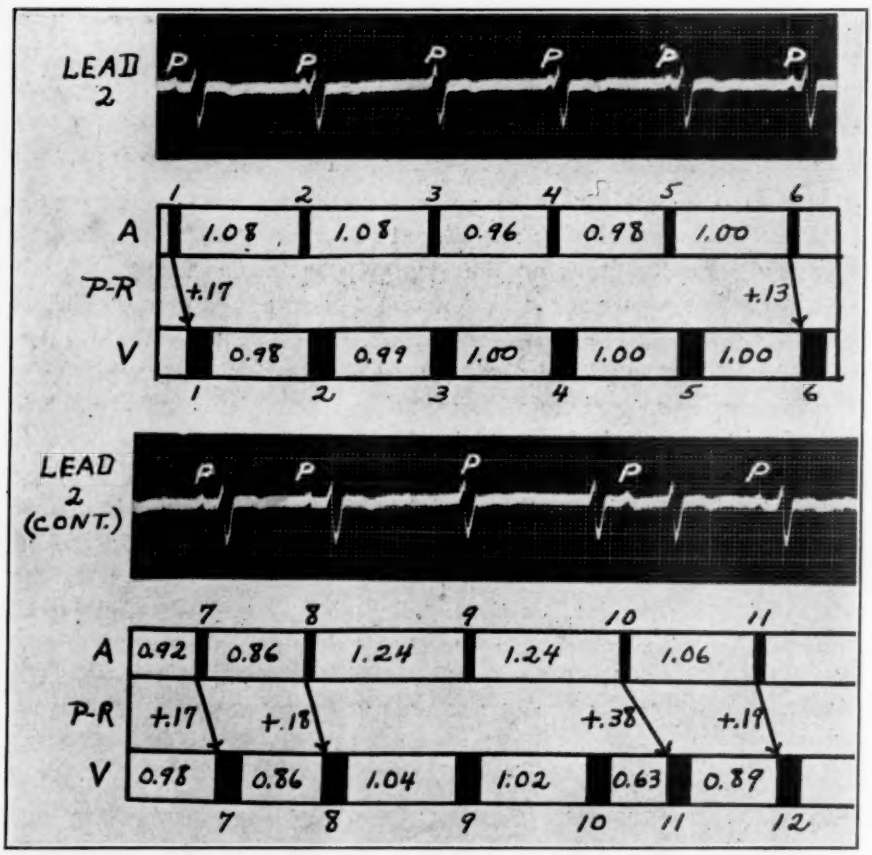

Fig. 2.—F. J. Continuous tracing in Lead II, Jan. 28, 1932. Of especial interest is the auricular beat 10 followed by ventricular beat 11 after a long P-R interval.

Electrocardiographic Findings.—The same type of rhythm abnormality shown here was present in Case 8 (Table I). The tracings in this second case have been published elsewhere[19] and will not be repeated here.

It should be noted at the outset that intraventricular block is present and that the T-waves are depressed, both being evidence of the serious myocardial disease present. At the beginning of the tracing it is observed that the A-A interval is longer than the V-V interval

(beats 1 and 2) and that the P-waves approach and merge into the QRS complex. At this time the control of the ventricular rhythm by the A-V node is greater than that by the S-A node and ventricular beats 2 and 3 are due to stimuli from the A-V node. At this point the S-A node speeds up for some reason and gradually returns to its normal position in front of the QRS complex. Thus by ventricular beat 6, or possibly 7, the S-A node is discharging its impulse sufficiently early so that the whole heart responds to it. However, after beat A-8, the S-A node suddenly slows up considerably and the ventricles again escape, A-9 falling within the QRS and A-10 following V-10. In fact A-10 falls at a time when the ventricles have partially recovered from their refractory period and the early beat V-11 is a response to A-10 after a considerably prolonged P-R interval. This long P-R interval is evidence that the conducting tissues are still partially refractory. After beat V-11, the S-A node speeds up somewhat and regains control of the heart for several beats. Nowhere in the tracing are there inverted P-waves following escaped ventricular beats, but this fact is not significant except after ventricular beats 10 and 11, especially the latter, when the auricles should no longer be refractory themselves to a stimulus arising in the A-V node. Hence the condition of retrograde block is present, at least after ventricular beat 11, and the (at times) slower S-A pacemaker is protected from the (at times) more rapid A-V node. Thus the S-A and the A-V nodes have at this time somewhere near the same rhythmicity (due in large measure probably to a depressed S-A node) and the S-A node, as it waxes and wanes, gains and then loses control of the heartbeat. This has been previously observed by Lewis.[18]

CASE 3.—(Case 3 in Table I.) V. H., a twenty-seven-year-old white, native, married waitress was admitted to the hospital on May 27, 1932, because of dyspnea and evidence of recurrent rheumatic fever. Her first attack of rheumatic fever had been at the age of four years, and she had had several recurrences since then.

The patient was quite ill at entry and had a fever of 103° F., which gradually subsided during the next two weeks. The physical findings of especial interest were limited to her heart. On June 7, 1932, she was examined by Dr. Marshall Fulton and the following description is extracted from his notes:

The heart rate was about 80, and the action was irregular. The impulse was diffusely felt over a wide area, and there was a striking difference in the intensity of the impulse with different beats. This was even more definitely brought out on auscultation. At times the first sound was soft and just audible; at other times it was very abrupt, loud and snappind. At the apex there was a low-pitched diastolic rumble, and at the base, a long diastolic murmur typical of aortic insufficiency. The heart was definitely enlarged. When the heart was irregular, the patient felt it "jumping" in her chest.

The patient gradually improved on bed rest and salicylates and was discharged July 3, 1932. She left town shortly after this and attempts at follow-up have been unsuccessful.

Electrocardiographic Findings.—This tracing is practically identical with that obtained in Case 2 (Table I), which will not be discussed

separately. The auricular rate is again slower than the ventricular (beats 2, 3, 4, etc.), and the condition of retrograde block is present, so that no impulses of A-V origin are conducted back to the auricles. However, it is observed that there is considerably less arrhythmia of the S-A node and that the rhythm of the A-V node is faster than in Fig. 2. Thus the fact that the two nodes have somewhere near the same rhythmicity is due, in considerable part at least, to enhanced irritability of the A-V node. By ventricular beat 4, at least, the ventricular pacemaker in the A-V node has escaped and continues to control the ventricular beat through beat V-10, the auricles responding unmolested to the S-A node. Auricular beat A-10 falls at a time when the ventricle is only partially refractory and so the ventricle responds after a long P-R interval, resulting in the quickened beat V-11. The interval between V-11 and V-12 is also considerably shortened. The explanation for this is to be found in the nearly normal P-R interval between A-11 and V-12, which occurs because A-11 falls at a time when the ventricle is no longer refractory. If the P-R interval between A-10 and V-11 were the same as between A-11 and V-12 (namely 0.21 sec.) the interval between V-11 and V-12 would be 0.77 sec. instead of 0.52 (0.46–0.21 = 0.25 and 0.52 + 0.25 = 0.77). Thus it is seen that V-11 occurs late because of the long P-R interval preceding it.

One other point worthy of comment is to be observed at the end of the tracing. When the S-A node has succeeded in regaining control of the heart, it speeds up for several beats, and the P-wave maintains its normal position in front of the QRS complex. This finding is present in several published electrocardiograms.[1, 8, 17, 20, 21, 22] After a short time, however (not shown in this illustration), the S-A node again slows down, and the whole process repeats itself. This tendency of the arrhythmia to recur at fairly regular intervals is known as allorhythmia.[18]

Why the S-A node often speeds up after it gains control of the entire heart is not clear. Possibly, as suggested by Zeisler,[23] the coronary blood flow, with subsequent better nutrition of the S-A node, may be maximal when the heart chambers are beating in their normal sequence. An apparently related phenomenon was observed by Wilson and Robinson[24] in complete heart-block. They noted that the interauricular intervals which contained a ventricular systole were often shorter than the interauricular intervals containing no ventricular beat.

CASE 4.—(Case 6 in Table I.) J. P., a nineteen-year-old, single, Italian unemployed girl, was admitted March 14, 1936, for the fifth time because of recurrent rheumatic fever. The first attack occurred at the age of seven years.

At entry she had a fever of 102° F., which persisted for nearly three weeks, gradually subsiding to normal. The significant physical findings were limited to her heart, which was moderately enlarged to the left as revealed by physical examination

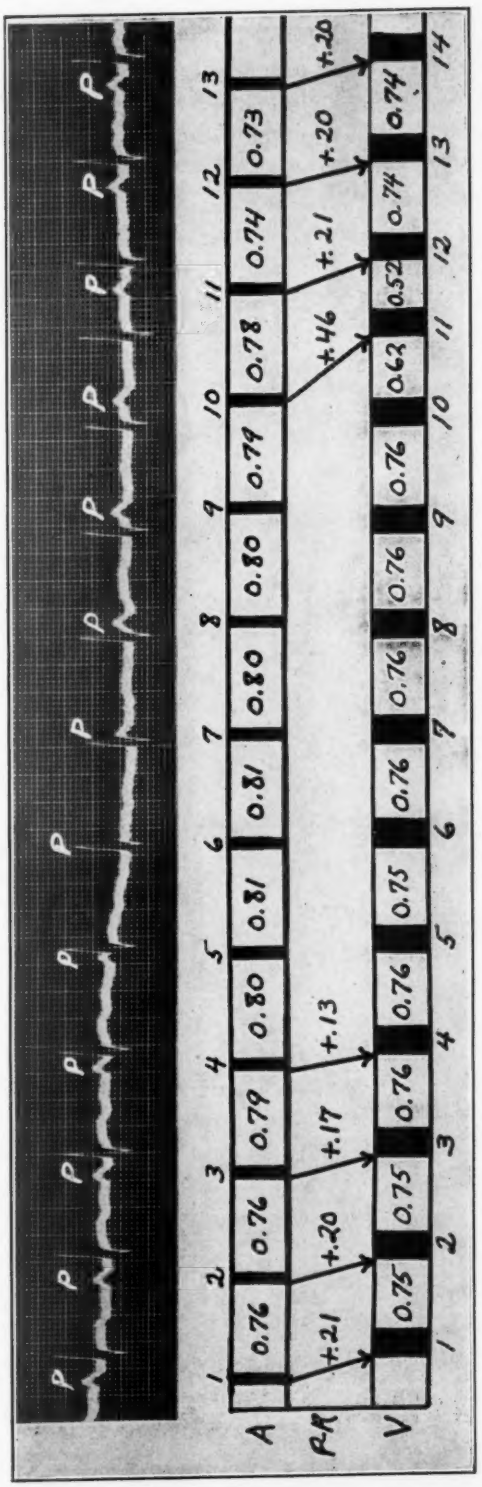

Fig. 3.—V. H. Lead II. June 15, 1932. Note the early ventricular beats 11 and 12, both of sino-auricular origin.

and by x-ray. There was a long blowing diastolic murmur to the left of the sternum, and the blood pressure was 136/30. There was an apical diastolic murmur present also, but the significant lesion appeared to be aortic regurgitation.

She gradually improved and was discharged May 1, 1936, for further rest at home. Unfortunately she was not carefully examined at the time when her heart was exhibiting the irregularity shown in the electrocardiogram, and so we do not know whether she showed variations in the first heart sound, as did the patient in Case 3.

Electrocardiographic Findings.—This is another example of interference dissociation and the abnormality here is very similar to that in Fig. 3. In the first part of the tracing the S-A node slows up, and the A-V node, being more irritable than normal, gains control of the ventricular beat. Retrograde block is present, and the auricular waves fall within and then to the right of the QRS. Finally, at beat A-7, the P-wave falls at a time when the ventricle is only partially refractory

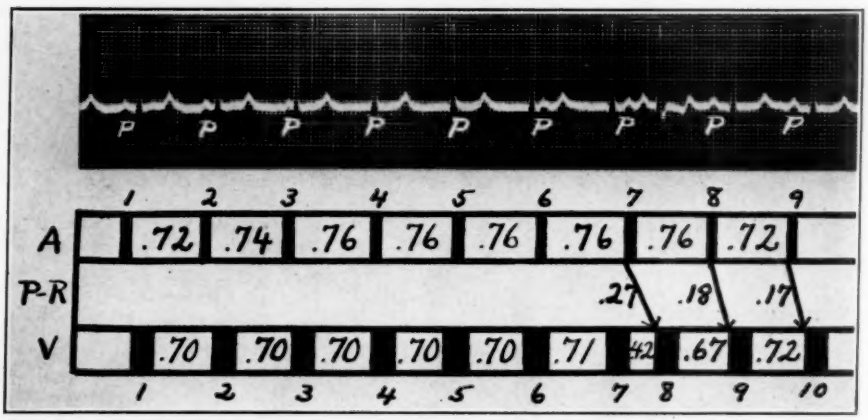

Fig. 4.—J. P. Lead II. March 27, 1936. Another example of interference dissociation. Note auricular beat 7 followed by ventricular beat 8 after a long P-R interval.

and a quickened beat V-8 results, after a long P-R interval. This ventricular complex is somewhat aberrant in form, probably because of some delay or variation in conduction of the impulse through the lower or more terminal portions of the ventricular conducting system. After the S-A node has gained control, it again speeds up for a few beats as in Fig. 3. The quickened beat V-9 has the same explanation as beat V-12 in Fig. 3.

This same patient has had many electrocardiograms taken during her several hospital entries. One taken Aug. 9, 1930, about six years before the one shown in Fig. 4, showed the P-wave approaching and finally merging into the QRS complex. In the short record taken at that time, the P-wave did not appear to the right of the QRS, and there was no interference dissociation. However, the A-V node was undoubtedly hyperirritable (the patient's temperature at this time was 102° F.) and

the same tendencies were undoubtedly present that are shown more strongly expressed in Fig. 4. Thus it is probable that this same arrhythmia may recur in the same patient after long intervals if the proper conditions are present.

CASE 5.—(Case 5 in Table I.) E. P., a twenty-one-year-old, male, Italian peddler, was admitted on July 30, 1935, because of painful, swollen joints of three days' duration. This was his initial attack of rheumatic fever.

His temperature at entry was 103° F., and remained about 102° F. for four weeks after entry. During this time he developed a pericardial friction rub followed by a rather large pericardial effusion. He had a moderately loud apical systolic murmur which persisted throughout his stay, except during the height of the effusion, when the heart sounds became practically inaudible. He was discharged Oct. 7, 1935, feeling well, and he was to remain at home in bed for two months.

He was examined at the time he was showing the electrocardiographic irregularities, and definite variations in the intensity of the first heart sounds were noted. The patient was of rather stolid nature and was not aware of any unusual sensa-

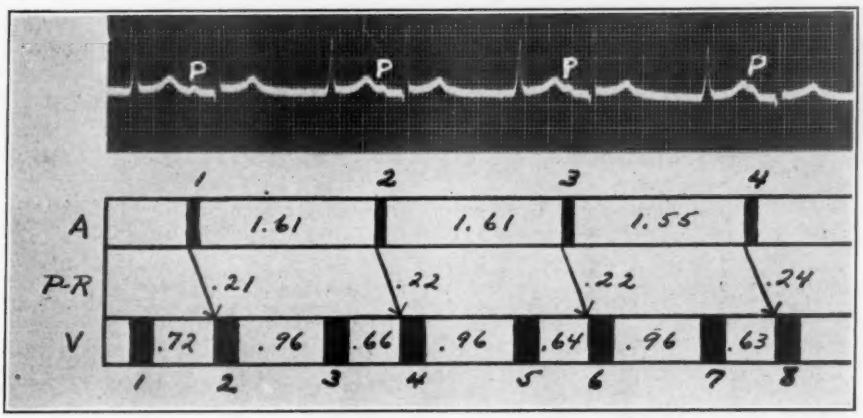

Fig. 5.—E. P. Lead II. Aug. 3, 1935. An unusual type of coupling with a slow auricular rate. Note the difference between the QRS complexes preceded by a P-wave and those with no preceding auricular wave.

tions himself. He was last seen on July 11, 1936. At that time he felt perfectly well. Examination of his heart was entirely negative. The rate was regular at 70, the size was normal to percussion, and there were no murmurs. There was no unusual pulsation of his chest wall and no distention of the neck veins to suggest significant pericardial involvement.

Electrocardiographic Findings.—This is one of several tracings taken on this patient. Several of these showed typical interference dissociation as shown in Figs. 2, 3, and 4. The one reproduced here was selected because it reveals an unusual type of coupling caused by the same mechanism as the arrhythmia in Figs. 2, 3, and 4. In the first place it is to be noted that there is some increase in the conduction time and that there is slight but definite elevation of the S-T interval. Both of these abnormalities are probably associated with the active rheumatic infection, the latter being due, in all probability, to the pericarditis. It is seen that the S-A node is underirritable and is discharging impulses

very slowly. The A-V node is definitely more irritable than the S-A node and gives rise to a ventricular beat (beats V-3, 5, and 7) at a fairly constant interval after the preceding beat of S-A origin (0.96 sec. in the above tracing). The auricular beats A-2, 3, and 4, because of the slow S-A rhythm, fall at a considerable interval after the preceding ventricular contractions, and hence the ventricle responds readily, being no longer refractory. There is no retrograde conduction.

Beats V-1, 3, 5, and 7 then are of A-V nodal origin, while beats V-2, 4, 6, and 8 are of S-A origin. These beats are seen to be different, those of A-V origin being lower and more slurred than those of S-A origin. This has been previously observed by others and is thought to be due to a slightly different path taken by the impulses of A-V origin.[1, 25]

CASE 6.—(Case 11 in Table I.) C. L., a sixty-six-year-old white, married, French housewife, was admitted Nov. 5, 1935, because of increasing dyspnea for the preceding six weeks. The onset of her disability followed a day of unusually hard housework. There had been some indefinite precordial oppression. While at home she had been taking an undetermined number of tablets, thought to be digitalis.

On physical examination she was seen to be quite ill. There were many râles throughout both chests. The heart was apparently enlarged, but there were no murmurs. The rhythm was regular at this time. The blood pressure was 220/140.

In the first electrocardiogram, taken Nov. 6, 1935, the rhythm was regular; there was left axis deviation; and the T-waves were upright in Lead I. In the fourth lead, however, the Q-waves were absent, but the T-wave was inverted normally. It was felt that she had hypertensive heart disease and probably coronary thrombosis of several weeks' duration. Medication consisted of digitalis gr. 1½ three times daily.

She remained about the same for four days and then quite rapidly developed a temperature of 102° F. She failed rapidly and died Nov. 11, 1935, apparently of a terminal bronchopneumonia. Autopsy permission was refused.

Electrocardiographic Findings.—This record was selected for reproduction because, though the waves are rather small and indistinct, it shows one variation of interference dissociation not present in any of our other patients. In this record there is an arrhythmia of the same type shown in Figs. 3 and 4. The A-V node is producing impulses quite rapidly and readily gains control of the ventricles for most of the tracing. There is no retrograde conduction, and beat V-6 is quite comparable to beat V-8 in Fig. 4 and beat V-11 in Fig. 3. There is very little difference in the QRS complex whether the beat originates in the S-A node or the A-V node. The point of especial interest in this record centers about beat A-9 and the interval between beats V-10 and V-11. It is seen that A-9 falls shortly after V-10 and is not followed by a ventricular response. However, the A-V node does not discharge an impulse after the usual interval (0.56-0.60 sec.), and the ventricle only responds after the next auricular beat (A-10). Thus it seems probable that beat A-9, although it did not evoke a ventricular response, has succeeded in discharging the A-V node and in destroying the impulse

that was in the process of being built up there. This might occur if we assume the presence of refractory conducting tissue below but not above the A-V node. These pauses in ventricular rhythm might be caused by a sudden change in the rhythm of the A-V node or by A-V nodal block (comparable to S-A block) independent of the auricular beat. However, our first explanation seems most reasonable because an identical break in rhythm occurred in two places in another tracing on this patient. In these pauses, the sequence of beats was exactly as illustrated in Fig. 6 (QRS→upright P-wave→beat of S-A origin). It seems most improbable that any independent variation in the rhythm of the A-V node would occur only in relation to a QRS complex followed by a P-wave—especially as this sequence (QRS followed by P) appeared only infrequently in the tracings.

The A-V node is thus delayed and does not give rise to another beat before the S-A node has discharged an impulse and taken control of the

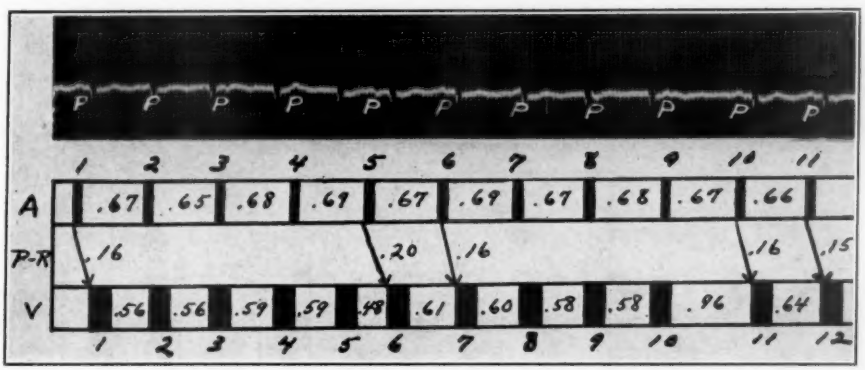

Fig. 6.—C. L. Lead I. Nov. 9, 1935. Especial interest in this tracing centers about the pause between ventricular beats 10 and 11. See discussion in text.

heart. A few beats after A-11, however, the A-V node regained control of the ventricular beat and the interference dissociation reappeared as in the beginning of the tracing.

COMMENT

One abnormality of rhythm not discussed or illustrated here, although closely related to those under discussion, is reciprocal rhythm, in which one retrograde auricular beat is sandwiched between two ventricular beats, one wave of excitation presumably traveling from the A-V node back to the auricle and then reentering the ventricle by some ill-understood path and producing a second ventricular beat. We have one patient, now being followed, who has shown this abnormality on several occasions. Since considerable discussion and several illustrations are necessary to present this patient's case adequately, it is planned to make him the subject of a subsequent report.

TABLE I

NO.	SEX AND AGE	CLINICAL DIAGNOSIS	CHANGES IN FIRST HEART SOUNDS	TEMPERATURE ON DAY OF EKG.	DIGITALIS	DATE OF EKG. AND VENTRICULAR RATE	COUPLED BEATS	DURATION OF IRREGULARITY	DATE LAST SEEN AND CONDITION
C. H. 1	M 21	Rheumatic fever	?	99.4	0	6/25/26 67	0	16± days	6/13/31 Dead
J. C. 2	M 15	Rheumatic fever	?	102.0	0	7/20/32 84	+	1± day	5/16/35 Fair
V. H. 3	F 27	Rheumatic fever	+	101.5	0	6/15/32 80	+	10± days	7/ 3/32 Fair (lost)
A. M. 4	F 11	Rheumatic fever	?	101.5	0	7/15/15 113	0	Few hours	12/16/15 Fair (lost)
E. P. 5	M 21	Rheumatic fever	+	102.0	0	8/ 3/35 74	+	9± days	7/13/36 Good
J. P. 6	F 19	Rheumatic fever	?	102.0	0	3/27/36 88	+	5± days	5/ 1/36 Poor
C. D. 7	M 22	Acute tonsillitis	+	99.0	0	5/27/32 54	0	4± days	5/31/32 Good (lost)
R. N. 8	F 27	Adrenal tumor	+	98.6	0	3/11/35 81	+	Few minutes	5/ 7/35 Dead
B. F. 9	F 37	? Paralysis agitans	+	98.6	0	11/20/34 46	0	15± days	5/ 4/35 Good
S. J. 10	M 67	Coronary thrombosis	?	99.2	0	12/15/32 79	0	?	1/ 9/33 Dead
C. L. 11	F 66	Bronchopneumonia	?	102.0	+	11/ 9/35 107	+	2± days	11/11/35 Dead
F. J. 12	F 69	Hypertensive heart disease	?	98.6	+	1/28/32 69	+	6± days	Oct., 1932 Dead

Table I contains a summary of some of the clinical data on these twelve cases, a portion of which seems worthy of further consideration. It is seen that six of the twelve patients suffered from acute rheumatic fever, and one other patient had acute tonsillitis—a related condition. So far as we know, previous reports on interference dissociation and A-V rhythm that have appeared in English have not mentioned rheumatic fever as an important cause. However, Oettinger and Neslin[8] described the occurrence of interference dissociation in seven patients with acute rheumatic fever. In a footnote they add that after subsequent observations they have noted its occurrence in fourteen out of 200 patients with rheumatic fever studied electrocardiographically. Such a high incidence of this relatively rare arrhythmia in patients with rheumatic fever certainly indicates that this disease must be considered an important predisposing factor in its production. Conversely, the occurrence of the electrocardiographic changes previously illustrated, especially in a young person, is highly suggestive of rheumatic infection. However, it should be mentioned that in our cases the rheumatic fever accompanying the arrhythmia was quite severe and easily recognizable by ordinary clinical observation.

Another apparently significant association was the relation of the arrhythmia observed to a febrile reaction. Thus, nine of the twelve patients had temperatures of at least 99° F. on the day the electrocardiogram showing the arrhythmia was taken. Six of these nine patients had temperatures over 101° F. Of the three patients showing no fever on the day of the electrocardiogram, one patient (Case 12) had just recovered from an attack of bronchopneumonia and had had a temperature of 102° F. a few days previously. Another (Case 9) had not had a temperature in the previous few days but had had a debilitating attack of grip about four weeks previously. The third patient (Case 8) was not observed to have an abnormal temperature but suffered from paroxysms of which marked transient hypertension was the most outstanding objective sign. In this latter patient, who was proved by operation to have a chromaffin cell tumor of the right adrenal,[19] the periods of marked generalized stimulation of the sympathetic system were probably to a large extent causative in inducing the arrhythmia.

Thus in the majority of these cases the association of the arrhythmia with concomitant active infection (Cases 1, 2, 3, 4, 5, 6, 7, and 11) or recent infection (Cases 9 and 12) seems significant. The slight fever in Case 10 was probably associated with recent coronary thrombosis, and the arrhythmia in this case is perhaps associated with faulty blood supply to one or both nodes. In the other cases mentioned above it would seem that infection, especially rheumatic infection, by direct involvement of the heart or perhaps (in nonrheumatic infections) by resulting toxemia, is an important factor in disturbing the rate of impulse

formation in the S-A and A-V nodes. The question may well be raised as to why this arrhythmia does not appear more often with rheumatic fever and infection. There are several possible answers, all speculative. Perhaps it may occur only when some inherent abnormality is present in one node or the other causing it to respond disproportionately or perversely to extraneous stimuli. Possibly, and this seems reasonable in view of what we know concerning rheumatic infection, it occurs when the rheumatic (or infectious) process is especially intense about one node or the other resulting in either stimulation or depression. However, such situations do not seem to occur ordinarily, and the usual result of infection is an increase in the rate of impulse formation of the S-A node, which thus continues to dominate the heart even if the A-V node has been correspondingly stimulated.

As regards contributory factors, comment should be made concerning the rôle of digitalis. Some authors[10, 23] have given much etiological importance to this drug in the production of this type of arrhythmia. It is undoubtedly of occasional importance, but it seems of considerable significance that only two of our twelve patients and none of Oettinger and Neslin's seven patients[8] received any digitalis prior to the appearance of the arrhythmia. Thus, in this group of cases at least, digitalis was of minor importance in the production of the arrhythmia. The patient in Case 12 was receiving only a maintenance dose of gr. 1½ daily and showed no other sign of digitalis intoxication. Case 11 had received 18 gr. in four days and perhaps more prior to entry to the hospital. That digitalis was of significance in producing the arrhythmia in these two patients cannot be denied, but it is our impression that its effect was, at the most, contributory.

Of the twelve patients, five were definitely observed to have changes in the intensity of the first heart sounds on the day when the electrocardiographic arrhythmia was present. This has been observed by others and Oettinger and Neslin[8] by means of a phonocardiograph were able to demonstrate an increased intensity of the first sound when the P-wave and QRS fell together or when the P-wave shortly preceded the QRS. This would be expected as there is a similar increase in the intensity of the first heart sound when the P-wave and QRS fall together in complete heart-block.[18] It is probable that all twelve of our patients would have shown this variation in the first heart sound if careful auscultation had been performed at the time when the arrhythmia was present.

Case 9 showed a sudden vigorous pulsation of the neck veins concomitant with the increased intensity of the first sound. More careful observation would probably have revealed this finding in several other cases. However, since this observation was not recorded in our other cases, we do not have satisfactory objective evidence of its frequent occurrence.

When these sudden intense first heart sounds occur, some patients complain of more or less palpitation. Its presence was definitely noted in Cases 3, 8 and 9. In Case 5 it was absent at the time loud beats were heard, even though the patient was specifically questioned in this regard. In the remaining cases, we do not have exact data regarding its occurrence. It is probable that the more sensitive patients feel these forceful beats, while less sensitive ones do not. The situation is thus comparable to the presence or absence of palpitation with extrasystoles. Wilson[17] had three patients who complained of intense palpitation during experimentally induced A-V rhythm.

As regards the duration of the irregularity, we have no precise data. A rough approximation of the upper limits of duration was arrived at by recording the time interval between the first record showing the arrhythmia and the first record in which it was absent—provided the records were taken at reasonably short intervals. By such means it seems that the irregularity may persist for from a few minutes (Case 8) to sixteen days (Case 1). In the average case it apparently lasts a few days. In Oettinger and Neslin's cases[8] the irregularity lasted usually from one to six days.

Follow-up studies, so far as possible, have revealed that five of the twelve patients are dead (Cases 1, 10, and 12, heart disease, and Case 11, heart disease complicated by bronchopneumonia). In Case 8 death in shock resulted shortly after operation for removal of the adrenal tumor.[19] Three patients (Cases 2, 3, 6) had evidence of advanced rheumatic heart disease when last examined. In Case 4 there was evidence of slight rheumatic heart disease at the last visit. Three patients (Cases 5, 7, and 9) had no definite evidence of heart disease when last studied. As regards the clinical significance of the arrhythmias observed in these patients, the conclusions of Richardson[26] concerning A-V rhythm seem distinctly applicable. He writes, "A-V rhythm is not in itself fatal, but is frequently associated with severe infection or severe and chronic cardiac disease." With this we agree.

SUMMARY AND CONCLUSIONS

1. Twelve patients are reported whose electrocardiograms showed the control of the ventricular beat changing frequently between the S-A node and the A-V node. The electrocardiograms of seven of these patients exhibited interference dissociation.

2. In order for these transitions to appear, the A-V node must become temporarily more irritable than the S-A node. Such a condition may occur (a) when there is considerable depression of the S-A node, (b) when there is increased irritability of the A-V node, and (c) when there is a combination of the two effects described in (a) and (b).

3. If, when the A-V node is more irritable than the S-A node, retrograde conduction to the auricles is possible, A-V rhythm results; if retrograde conduction is blocked, interference dissociation appears.

4. In a given instance of this arrhythmia the auricular rate is usually more variable than the ventricular rate.

5. When control of the ventricular beat varies between the nodes, the QRS complexes may or may not show differences between beats of S-A and A-V origin.

6. Evidence is presented strongly suggesting that the S-A node may discharge a partially formed impulse in the A-V node without a resultant ventricular response.

7. Active rheumatic fever was present in six of our twelve cases and can be an important predisposing factor in the production of the arrhythmias under discussion.

8. Nine of our twelve patients had abnormally high temperatures on the days that the electrocardiograms showing the arrhythmias were taken.

9. Ten of the twelve patients had no digitalis prior to the appearance of these transitions in rhythm.

10. Subjectively these arrhythmias are frequently associated with palpitation and objectively with changes in the intensity of the first heart sounds, with coupled beats, and, at times, with sudden vigorous pulsations of the neck veins.

11. In the average case this abnormality in rhythm lasts a few days.

12. Seven of our twelve patients showed evidence of serious heart disease.

NOTE: It is a pleasure to express our indebtedness to Dr. Paul D. White for constructive criticism in the preparation of this paper.

REFERENCES

1. Pardee, H. E. B.: Clinical Aspects of the Electrocardiogram, New York, 1933, ed. 3, Paul B. Hoeber, Inc.
2. White, P. D.: Clinical Observations on Unusual Mechanisms of the Auricular Pacemaker, Arch. Int. Med. **25**: 420, 1920.
3. White, P. D.: The Bigeminal Pulse in A-V Rhythm, Arch. Int. Med. **28**: 213, 1921.
4. Sherf, D., and Shookhoff, C.: Further Studies on Conduction in the His Bundle, AM. HEART J. **2**: 48, 1926.
5. Personal unpublished observations.
6. Mobitz, W.: Zur Frage der atrioventrikularen Automatie, Deutsches Arch. f. klin. Med. **141**: 257, 1923.
7. Herrmann, G., and Ashman, R.: Interference Dissociation in Contrast to Reciprocating Rhythm, Proc. Soc. Exper. Biol. & Med. **28**: 264, 1930.
8. Oettinger, I., and Neslin, W.: Über Atrioventrikulare Automatie bei Rheumatischer Karditis, Deutsches Arch. f. klin. Med. **173**: 212, 1932.
9. Jones, T. D., and White, P. D.: A-V Nodal Rhythm; Report of Two Cases Exhibiting Bigeminy, AM. HEART J. **2**: 226, 1927.
10. White, P. D.: Ventricular Escape With Observations on Cases Showing a Ventricular Rate Greater Than That of the Auricles, Arch. Int. Med. **18**: 244, 1916.
11. Wilson, F. N.: Three Cases Showing Changes in the Location of the Cardiac Pacemaker, Associated With Respiration, Arch. Int. Med. **16**: 86, 1915.

12. Hewlett, A. W.: Case Showing Rapid Ventricular Rhythm With Periods of A-V Dissociation, Heart **10:** 9, 1923.
13. Kerr, Wm.: Nelson's Loose Leaf Medicine, Vol. **4:** 640-0.
14. Gallavardin, L., Dufourt, P., and Petzetakis: Automatisme ventriculaire intermittent spontane ou provoque par la compression oculaire et l'injection d'atropine dans les bradycardies totales, Arch. d. mal. du coeur **7:** 1, 1914.
15. Resnik, W. H., and Lathrop, F. W.: Changes in the Heart Rhythm Associated With Cheyne-Stokes Respiration, Arch. Int. Med. **36:** 229, 1925.
16. Dressler, W.: Zur Frage der Entstehung der Interferenzdissoziation und der retrograden Fortleitung ventrikularen Extrasystolen, Wien. Arch. f. inn. Med. **19:** 611, 1930.
17. Wilson, F. N.: The Production of A-V Rhythm in Man After the Administration of Atropine, Arch. Int. Med. **16:** 989, 1915.
18. Lewis, T.: The Mechanism and Graphic Registration of the Heart Beat, ed. 3, London, 1925, Shaw & Sons, Ltd.
19. Burgess, A. M., Waterman, G., and Cutts, F. B.: Suprarenal Sympathetic Syndrome With Cardiac Changes Resulting from Pheochromocytoma of the Right Suprarenal, Arch. Int. Med. **58:** 433, 1936.
20. Blumgart, H. L., and Gargill, S. L.: The Mechanism of Transitions from A-V Dissociation to S-A Rhythm; Its Relation to the Theory of Parasystole, Am. Heart J. **5:** 437, 1930.
21. Marcellus, M. B.: Migratory Pacemaker, With Report of Case Including Autopsy Findings, Northwest. Med. **33:** 189, 1934.
22. Goodman, M.: Mechanisms of Cardiac Rhythm Illustrated by Unusual Human Electrocardiograms, Am. J. Med. Sc. **189:** 657, 1935.
23. Zeisler, E. B.: A-V Dissociation, J. Lab. & Clin. Med. **18:** 225, 1932.
24. Wilson, F. N., and Robinson, G. C.: Heart Block: Two Cases of Complete Heart Block Showing Unusual Features, Arch. Int. Med. **21:** 166, 1918.
25. Friedlander, R. D., and Kerr, W. J.: The Clinical Diagnosis of Tricuspid Stenosis. Report of a Case Complicated by Paroxysmal Nodal Tachycardia and A-V Dissociation, Am. Heart J. **11:** 357, 1936.
26. Richardson, H. B.: A-V Rhythm and Digitalis, Arch. Int. Med. **29:** 253, 1922.

CONSTRICTION OF THE PULMONARY ARTERY BY ADHESIVE PERICARDITIS*

BENJAMIN A. GOULEY, M.D.
PHILADELPHIA, PA.

ADHERENT pericardium has recently attracted considerable attention because of the realization that certain types of the lesion are amenable to surgery.[1, 2] The physical signs and the disturbance in circulatory function produced by pericardial adhesions may be attributed to either constriction or traction of the heart structure. The heart may be generally involved or the disabling effect may be exerted locally on one of the cardiac chambers or upon the great vascular trunks leading to or away from the heart. Thus, two important types that have been accorded clinical distinction are: (1) the constricting adhesive pericarditis, which affects practically the whole heart, especially the ventricles, and causes "failure of diastolic filling"; and (2) constriction of the inferior vena cava with resulting prolonged circulatory failure of the lower half of the body. A third type, rarely seen but equally distinct, is constriction of the superior vena cava with venous congestive failure of the upper half of the body.

Another involvement, which is the subject of this report and which has not been described in the literature as far as we know, is that which affects the pulmonary artery. The adhesions which at times surround this artery may be very dense and may actually compress and narrow the vessel to a striking degree. They are almost certainly the cause of physical signs which in our opinion are sufficiently definite to warrant a clinical diagnosis of pulmonary arterial constriction.

We wish to describe these signs, which are mainly demonstrable in the pulmonary area, and the underlying pathological lesions observed in five patients. We have also included clinical notes on a patient who has survived and who presents physical signs identical with those noted in some of the cases which came to necropsy.

CASE 1.—C. F., twelve years old, negress, had a severe attack of rheumatic fever two years previously, during which pneumonia had been present and involvement of the heart had been recognized. After some months of inactivity, the process again became active. The severity of this attack, which was again complicated by pneumonia, led to her admission to the Medical Service of Dr. Howard Schaeffer, Philadelphia General Hospital, on April 22, 1933. She presented the typical picture of a severe, active rheumatic fever with painful swelling of the large joints, elevated temperature, and considerable substernal and precordial pain.

The heart was greatly enlarged, the transverse diameter being 18.5 cm. by roentgen examination (Dr. C. Burvil Holmes). At the apex there was a blowing systolic

*From the Departments of Cardiology and Pathology, Philadelphia General Hospital, and the Robinette Foundation, University of Pennsylvania.

murmur. The findings we wish to emphasize were those present at the base of the heart, mainly to the left of the sternum. These were (1) increased widening of the cardiac dullness in the second and third interspaces; (2) a marked systolic murmur and thrill; (3) a diastolic shock and marked accentuation of the second pulmonic sound; and (4) a striking wavelike systolic pulsation spreading upward along the left border of the sternum in the second and third interspaces and followed immediately by retraction. Although adhesive pericarditis was suggested by the marked cardiac enlargement and immobility of the apex, there was no systolic retraction except that noted in the pulmonary area. The remaining findings and laboratory data will be omitted except to note that the electrocardiogram showed, among other changes, prolonged P-R intervals.

The temperature ranged between 98° and 103° F. The patient became increasingly toxic and soon after, developing an encephalitis, died on May 12, 1933.

Necropsy (Dr. Bevan).—The heart was found to be greatly enlarged, the left ventricle and the auricles being considerably dilated; the right ventricle and conus showed definite hypertrophy but were only slightly dilated. The mitral valve was the seat of an acute and relatively slight endocarditis, being only very slightly thickened and not at all deformed. Along its free edge, there was a fine line of verrucous fibrinous deposit. The remaining valves were uninvolved and therefore furnished no explanation of the physical signs found at the base of the heart. These are to be explained by the adhesive subchronic mediastinopericarditis, which was particularly heavy and shaggy over the anterior aspect of the right ventricle and conus. The involvement extended well up along the course of the pulmonary artery surrounding and definitely compressing this vessel. This adhesion also actually compressed the pulmonic conus preventing dilatation, and at the same time securely fixed both conus and artery to the overlying chest wall.

Histology.—The appearance of the heart muscle from various chambers will not be described except to say that there was evidence of chronic and also subacute myocardial involvement. The pericardium surrounding the pulmonary artery and left auricle was enormously thickened, measuring as much as 1 cm. The outer portion consisted of rather loose and edematous connective tissue, greatly capillarized and showing rather numerous perivascular collections of lymphocytes. In the inner portion, the cellular activity was more pronounced, the collections of lymphocytes being augmented by small numbers of large mononuclears and plasma cells.

CASE 2.—M. B., a white woman, aged twenty-seven years, had been known to have aortic valvulitis and mitral stenosis for many years as a result of a severe rheumatic infection in early childhood. In spite of this, her health had been good until late in pregnancy, which was terminated by cesarean section. Immediate postoperative recovery was apparently satisfactory; however, early in the puerperium, heart failure developed and progressed to such a degree that hospitalization became necessary one month after delivery, the patient being admitted on May 1, 1934, to the Medical Service of Dr. Bernard Kohn of the Jewish Hospital, who kindly gave me permission to include this case in my series.

On admission, the patient was very weak, dyspneic, and cyanotic. Auricular fibrillation was now noted for the first time; and the liver and the lung bases were congested. There was a definite phlebitis of the right saphenous vein and also a swollen right arm, secondary presumably to thrombosis of the right subclavian vein. In addition to the obvious mitral stenosis and aortic insufficiency, we wish to emphasize these findings: a definite systolic thrill with a loud systolic and soft diastolic murmur present in the second and third interspaces—well out to the left of the sternum—which led to a clinical diagnosis of pulmonary stenosis and regurgitation.

The severe heart failure showed little response to treatment, and the patient died suddenly on May 7, 1934.

Necropsy.—Necropsy examination revealed advanced rheumatic heart disease, multiple pulmonary infarctions, marked passive congestion of the viscera, leg edema, ascites, and edema of the right arm.

The heart was greatly enlarged and the pericardial sac completely obliterated by widespread adhesion; there were many mediastinal adhesions attached anteriorly and laterally to the thoracic cage, the left lung, and the diaphragm. The pericardial adhesions were seen to encroach to a marked degree on the superior vena cava; and they were dense also over the anterior aspect of the right ventricle, but

Fig. 1.—Case 2. Showing unusually thick (13 mm.) pericardial adhesion around the pulmonary artery (*P.A.*); arrows point to the outer layer of the adhesion which everted on opening the conus and artery with subsequent release of tension. The artery is constricted, especially to its upper portion. Note at that level the thickness of tissue separating the artery from the aorta (*A*), marked by double pointed arrow. The pulmonary valve is moderately compressed; the conus (*P.C.*), hypertrophied.

were thickest over the pulmonary conus and artery where they measured 1.3 cm. (Fig. 1). The pulmonic ring was only slightly compressed, but the artery was so narrowed that, at 2.5 cm. above the valve, the index finger could not be inserted.

The mitral, aortic, and tricuspid valves all showed an advanced stenosis. Examination of the superior vena cava showed not only severe constriction due to surrounding pericardial adhesions, but almost complete occlusion above the constriction by an organized thrombus which extended into the right innominate vein.

Both lungs were rather small, gray, and emphysematous, and presented a number of hemorrhagic infarctions. The pulmonary artery exhibited mild atheromatous changes in the larger branches.

The histological examination showed only chronic myocardial changes as seen in old rheumatic hearts and will not be detailed. Sections through the thickened pericardium revealed no evidence of acute change but only old, completely organized fibrotic lesions.

CASE 3.—D. B., an eighteen-year-old negress, had satisfactorily recovered from her initial attack of rheumatic fever in 1929. She was not troubled by the resulting heart lesions until active rheumatic fever again appeared following an acute respiratory infection in October, 1931. Soon after the onset of this illness, she was

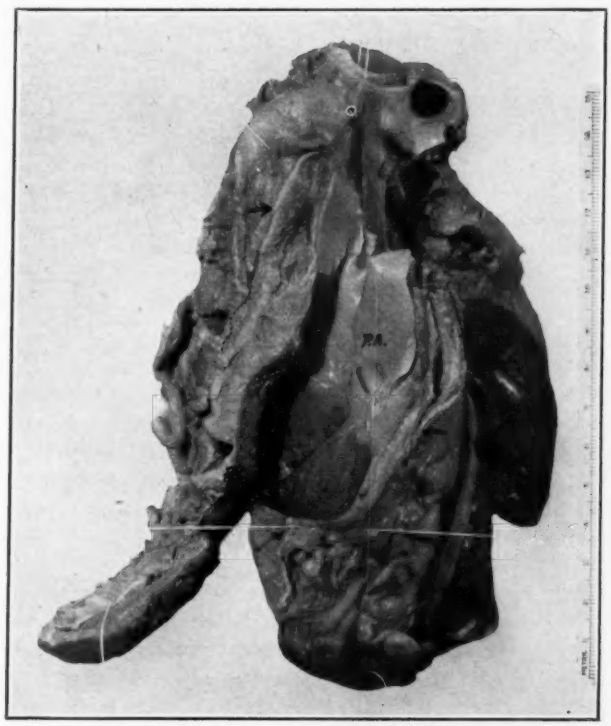

Fig. 2.—Case 3. Showing unusually thick pericardial adhesion surrounding the pulmonary artery (*P.A.*). The outer surface of the adhesion is shown by arrows and partly outlined by dotted line. The conus (*P.C.*) is hypertrophied and dilated. The valve ring and the first inch of the artery were unaffected, but the upper portion of the vessel was constricted.

admitted to the Medical Service of Dr. F. Kalteyer. On admission, the patient was obviously ill, being breathless, febrile (temperature, 101° F.), and miserable because of substernal pain. The heart was found greatly enlarged by percussion and roentgen ray examination (Dr. C. F. Nichols), and showed straightening of the left border with a prominent conus arteriosus and some widening of the base. Systolic and presystolic murmurs were present at the apex, and an unusually loud systolic murmur was heard over the second and third left interspaces, followed by a greatly accentuated second pulmonic sound. The various laboratory data will not be presented. After a stormy course, during which pneumonia developed, the patient died on April 10, 1932.

Necropsy (Dr. G. Robson).—There was a marked mediastinopericarditis. The pericardial cavity was closed anteriorly and laterally by very thick adhesions which were most conspicuous over the hypertrophied right ventricle and surrounding the pulmonary conus and artery, and definitely compressed the latter (Fig. 2).

The mitral valve presented a valvulitis with a semirigid, thickened rim affording some degree of obstruction; the aortic leaflets were also moderately thickened.

Histology.—A section of the left auricle and of the adhesive pericarditis showed great thickening of the pericardium, which had developed in at least three well-defined zones of recurring pericarditis. The outermost zone consisted of a loose, rather edematous connective tissue in which there was a scattering of fibroblasts and "epithelioid cells." The second zone consisted of a more compact fibrous tissue, much of which had undergone fibrinous degeneration and which was infiltrated with large basophilic cells, arranged either in Aschoff bodies or else massed in more or less parallel rows together with "epithelioid cells," in the manner described as "palisading."

The third and innermost layer consisted of a fairly dense connective tissue, which was markedly capillarized, and showed occasional perivascular collars of lymphocytes.

The auricular muscle showed a swelling of the individual fibers, a moderate interstitial edema, and a slight increase in the interstitial connective tissue. The small arteries and the arterioles showed a marked thickening of their wall, due mostly to intimal proliferation. Typical Aschoff bodies were present in the auricular myocardium.

CASE 4.—D. H., a negress, aged fifteen years, was admitted to the Philadelphia General Hospital, service of Dr. Henry Jump, on Dec. 29, 1932. Although she had had chorea in 1929, followed by the development of signs of heart disease, she had remained well until four weeks before admission, when an upper respiratory infection was followed by polyarthritis and substernal pain; she became very dyspneic and developed a high irregular fever.

Examination of the heart showed a moderate enlargement to the left, with a definite increase of dullness in the area of the pulmonary artery. There was a loud, blowing, systolic murmur at the apex, transmitted to the axilla. In the third and fourth interspaces to the left of the sternum, but heard also to a lesser degree along the entire border of the sternum, was a harsh, to-and-fro double murmur. There was a systolic thrill in this area, and P_2 was greatly accentuated.

X-ray examination (Dr. H. Ostrum) showed a thickening of the right interlobar pleura and right basal congestion. The heart was enlarged in its transverse diameter (cardiothoracic ratio being 14:23 cm.). The left auricle was enlarged, the left ventricle as well. There was considerable bulging in the left upper border of the heart due to an enlarged pulmonic conus.

The laboratory findings were as follows: erythrocytes, 3,700,000; hemoglobin, 55 per cent; leucocytes, 19,500.

The patient died on January 13 with acute rheumatic pancarditis and bilateral fibrinous pleuritis.

Necropsy.—The exopericardium was reddened and in some places covered with fibrinous exudate, lightly glued to the mediastinal pleura. There was an extensive plastic pericarditis, unusually heavy and tenacious around the base of the heart. The root of the pulmonary artery was definitely constricted by a mass of recently formed adhesions.

Section of the heart showed a slightly hypertrophied left ventricle while the right ventricle was markedly dilated. The muscle of both ventricles showed an acute,

parenchymatous degeneration. The mitral valve measured 6.5 cm.; the mitral rim was slightly stiffened and its line of closure studded by closely set, translucent verrucae.

The other valves were normal.

Histology.—Histological examination shows a subacute fibrinous pericarditis. There was a dense, almost diffuse infiltration of lymphocytes, endothelial cells, and also polymorphonuclears, in a fibrinous exudate showing early organization. Sections of left auricle and left ventricle showed a rheumatic myocarditis including well-defined Aschoff bodies.

CASE 5.—J. G., a negro child aged six years, whose case is not being presented in detail because both the clinical and the pathological pictures repeat the data brought out by the preceding cases, presented the picture of a severe, acute rheumatic fever, with striking physical signs in the pulmonic area (the most striking of which was a loud systolic murmur), which it is believed were the result of constriction of the pulmonary artery by the thick, fleshy, basal pericardial adhesions, found at necropsy. Incidentally, the orifice of the inferior vena was also considerably obstructed by adhesive pericarditis.

CASE 6.—F. M., a negro aged thirty-three years, who had had rheumatic fever in childhood, was admitted to the Medical Service of Dr. F. Kalteyer, Philadelphia General Hospital, because of severe heart failure, manifested chiefly by marked breathlessness and a swollen abdomen.

On examination, the evidences of heart failure were obvious, there being an enlarged, tender liver, considerable ascites, pulmonary congestion, and breathlessness. In addition to an apical systolic murmur, there was a harsh systolic murmur progressively louder in the fourth, third, and second left interspaces, which was followed by a marked accentuation of P_2 and a palpable diastolic shock, accompanied by a systolic thrill. In the area of the systolic thrill and murmur, there was a rather striking systolic pulsation which was immediately followed by retraction.

Fluoroscopic examination (Dr. C. F. Nichols) revealed widening and increased pulsations of the pulmonary artery, and visible adhesions between the base of the heart and that portion of the overlying chest wall which was the site of the systolic retraction, the thrill, and the murmur. These observations led us to feel that adherent basal mediastinopericarditis with constriction of the pulmonary artery was the most likely cause of the unusual physical signs, and that the large liver and ascites might well be ascribed to secondary right heart failure.

The patient ultimately recovered sufficiently to leave the hospital; his further course is not known.

DISCUSSION

Within the last few years, there has been an increasing interest in the physical signs and the radiological aspects of the pulmonic area of the heart, which previously had been largely neglected because of the conviction that physical signs in that area were of functional origin. This latter viewpoint is now undergoing change. Studies, both anatomical and clinical, indicate the presence of pulmonary arterial hypertension in certain types of disease.[3] Constricting basal pericarditis, involving the pulmonary artery, is an uncommon but apparently very effective cause of such hypertension.

Etiology.—The pericardial lesion herein described was caused by rheumatic fever. We have seen at necropsy a few cases of healed tu-

berculous pericarditis, where the pulmonary artery, in common with the rest of the heart, was surrounded by adhesions, but constriction did not exist to the degree noted in these rheumatic cases. Partial compression of the pulmonary artery by large, conglomerate, caseous lymph nodes in association with adhesion was noted in a patient not included in this report because of incomplete clinical data. Other factors may possibly be of etiological importance, but thus far in our experience, rheumatic pericarditis is the outstanding cause.

The Pathological Changes.—The fundamental pathological lesion is a massive mediastinopericarditis, in which thick adherent scar tissue surrounds and constricts the pulmonary artery. In the adult heart, as in the adolescent, the index finger is readily passed through the pulmonary artery up to its bifurcation, but in the cases herein described, this was often impossible. The constriction becomes notable as a rule about 2 cm. above the valve; in one instance, the vessel at its bifurcation was so narrow that a pencil could not be inserted into the origins of the two main branches. The width of these adhesions, which are often fleshy and somewhat edematous, is striking. In four cases they were from 10 to 15 mm. or more in thickness, and in three instances they completely filled in the anterior chest wall for a considerable distance (Fig. 3, *A* and *B*). The artery is possibly drawn forward toward the sternum; it appears, however, in some of the cases that the vessel is fixed or "frozen" in its normal position. Cross-section of the surrounding adhesion may reveal two or three inflammatory layers of different degrees of chronicity, indicative of recurring pericardial inflammation.

The pericarditis is seldom limited to the pulmonary artery. In only one patient (not included in this report) was there such localization. It may be the most conspicuous part of a universal pericardial adhesion, or it may be part of a pericarditis limited to the anterior aspect of the heart. It was not surprising, therefore, to find evidence, in some of the cases, of constriction of other vascular trunks. None of the group presented a typical picture of the Pick syndrome, but necropsy revealed marked constriction of the inferior vena cava in one case. In another there was superior vena caval obstruction. The superior vena cava was constricted by pericardial adhesions, and above the stenosis was a partially occluding thrombus. It is, therefore, evident that the patient who presents signs of pulmonary constriction may also have the picture of superior or inferior vena caval obstruction or of generalized pericardial adhesions. In one case the systemic aorta was partially constricted; as far as we know, there is no reliable method of recognizing this lesion.

All of these hearts showed rheumatic valvular disease. In Case 2 there was advanced mitral stenosis, but in four of the five cases which went to necropsy, the valve lesion was relatively mild, and in one

patient it consisted of a very recent verrucous endocarditis without previous disease. In this instance the pericardial lesion had preceded the valvulitis probably by many months.

Hypertrophy of the right heart was present and notable in every patient except in Case 4 (D. H.) in whom the process, consisting of a subacute fibrinous thickening with only recent organization, evidently was not old enough for the development of marked, right ventricular hypertrophy. Since the valve lesions were early and moderate in degree (except in Case 2), we believe that the right ven-

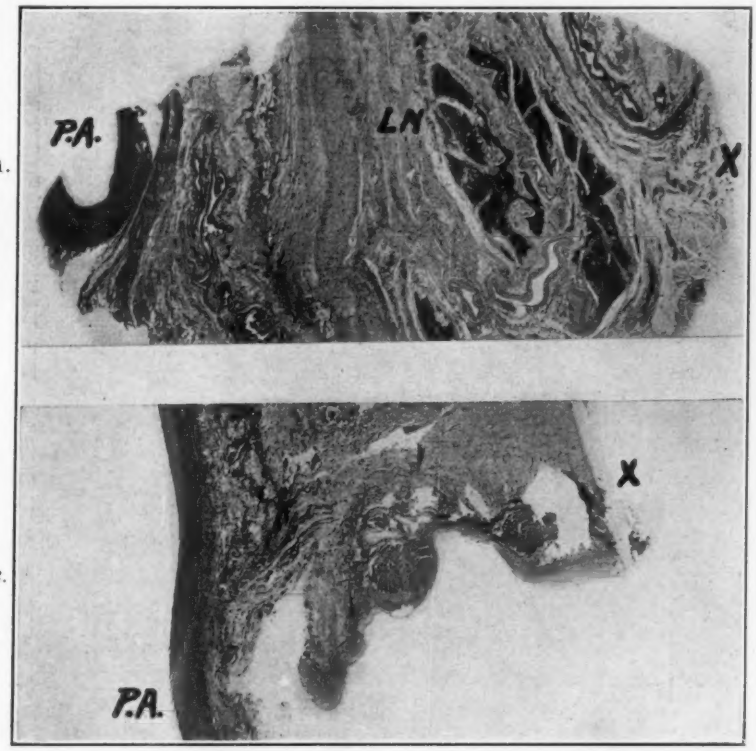

Fig. 3.—Case 3. *A*, Showing a small arc of a cross-section of the wall of the pulmonary artery (*P.A.*), and the massive adhesion which surrounds it and extends to the chest wall; *L.N.* indicates the remains of a mediastinal lymph node; *X*, the rough edge of the adhesion torn away from the anterior chest wall. *B*, Same as above, but in longitudinal section.

tricular hypertrophy is to be explained as one of the results of constriction of the main trunk of the pulmonary artery. It is the result of a proximal, localized pulmonary hypertension, analagous to the proximal, aortic hypertension and secondary hypertrophy of the left ventricle, associated with coarctation of the aorta. Although rheumatic pneumonitis[4] was present in the majority of these cases, marked pulmonary atherosclerosis was seen only once, in Case 2, in association with mitral stenosis. The absence of more pronounced pulmonary

arteriosclerosis and mitral stenosis is probably to be explained by the fact that four of the five cases which went to necropsy were young subjects who did not survive the rheumatic process sufficiently long to develop these changes.

Histological examination of the pulmonary artery in two cases (Cases 3 and 5) revealed a focal degeneration in the media, involving both muscle and elastic tissue. In a number of fields, the smooth muscle nuclei had either disappeared or stained poorly, and lay in a background of mucoid substance similar to that seen in certain degenerations of the aorta. In some places there was considerable

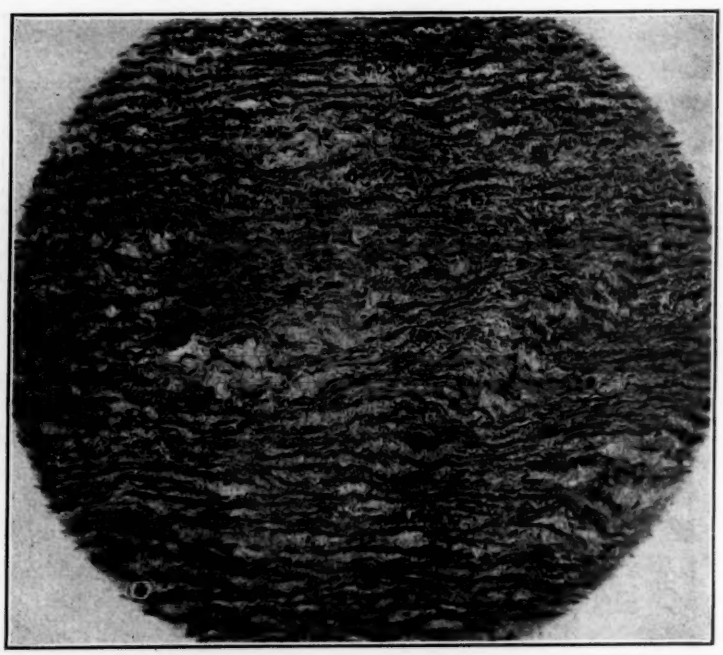

Fig. 4.—Case 5. Focal atrophy in the media of the pulmonary artery. Note disrupted rows of muscle nuclei, focal loss of nuclei, the frothy appearance, and the separation of the rows of the nuclei by a myxoid (?) infiltration. (×151.)

vacuolization between the disrupted rows of muscle nuclei, giving a frothy appearance to the already "moth-eaten" degeneration of the media (Fig. 4). We presume in the absence of cellular infiltration that this is a degenerative rather than an infectious process. The partial fixation of the pulmonary artery and the compression by the surrounding adhesions probably are factors in this focal atrophy of the media.

The Physical Signs.—Examination of the pulmonic area, employing the routine methods of inspection, palpation, percussion, and auscultation, will reveal a variable number of the following physical signs: (1) a harsh systolic murmur in the pulmonic area, in the second and

third left interspaces; (2) a greatly accentuated second pulmonic sound; (3) a diastolic shock in the same area; (4) a systolic pulsation coincidental with the systolic murmur, extending upward in the third and second left interspaces in the direction of the pulmonary artery, which may be followed by (5) a successive retraction of those interspaces, the whole process of pulsation and retraction having a striking sinuous appearance when well defined and seen in a favorable light; (6) the presence in a few cases, but of great importance when obtainable, of a systolic thrill palpable in the area of the systolic murmur and pulsation; (7) increase in the area of cardiac dullness in the third left interspace indicative of hypertrophy and dilatation of the right ventricle (conus portion).

When all of these signs are demonstrable in a given case, the picture is characteristic, and the diagnosis is not difficult. However, as reference to the protocols will show, there may be considerable narrowing of the pulmonary artery by pericardial adhesions without detection of all these signs by physical examination. In those cases that first came under our observation, some of these signs may have been present but were not thought of and consequently were missed. Systolic murmur, accentuated second pulmonic sound, and diastolic shock were present in all cases. Systolic murmurs in the pulmonic area are common and usually are not regarded as important. In these six cases, however, the murmurs were distinctly louder and rougher and heard over a more considerable area than the usual incidental pulmonic murmur, and therefore directed our attention to the existence of a lesion in this area. Systolic thrill was palpable in two instances. Its significance, of course, depends on its association with the other physical signs. Systolic pulsation and retraction in the pulmonic area are very suggestive, but do not constitute in themselves a pathognomonic sign; the retraction can be regarded as having the same significance (and with the same limitations) as the systolic retractions of adherent pericardium noted in other thoracic areas. At times it has proved difficult to be certain whether one is seeing a real retraction or the normal recoil following vigorous pulsations of a pulmonary artery lying relatively close to the chest wall.

In the light of the pathological findings, the physical signs can be reasonably classified on a physiological basis. The systolic murmur and systolic thrill are produced by the compression of the artery; hypertrophy of the right ventricle, especially the conus, the accentuated second pulmonic sound, and diastolic shock can be correlated with right ventricular hypertension and proximal hypertension of the pulmonary artery; the systolic pulsation followed by retraction is indicative of the attachment of the conus and even the pulmonary artery to the chest wall. There is a certain degree of overlapping in the physiological grouping of the physical signs; for example, the systolic

murmur may be attributed not only to compression of the artery, but also to the presence of pulmonary hypertension. We assume the existence of right ventricular hypertension in these cases, a conception that is now generally accepted in all types of pulmonary arterial obstruction, not on the basis of actual physiological observation (of which there is none) but on the more indirect evidence of hypertrophy and dilatation of the outflow portion of the right ventricle.

Differential Diagnosis.—Since no one sign is pathognomonic and since some of the signs, particularly those related to right ventricular hypertension, are to be seen in other disease processes, the diagnosis of stenosis of the pulmonary artery by pericardial adhesion often presents considerable difficulty. Inasmuch as rheumatic fever is the chief cause of this type of constricting pericarditis, the history of such infection and the presence of other cardiac lesions due to rheumatism will be of diagnostic help. Likewise, since the involvement of the pulmonary artery is usually a part of a more extensive pericarditis, other evidences of adhesions in the form of characteristic retractions, fixation of the apex beat, pulsus paradoxus, etc., may add some diagnostic corroboration. Two conditions that immediately enter the diagnostic problem are mitral stenosis uncomplicated by pericarditis and congenital pulmonary stenosis. Although right ventricular hypertrophy and pulmonary hypertension are prominent features in mitral stenosis, the other striking physical signs (of pulmonary arterial compression and adhesion) are not present. In congenital pulmonary stenosis, systolic murmurs and thrills are striking, but chest wall pulsations and retractions are not seen, and the second pulmonic sound is, as a rule, diminished. The many other conditions that produce pulmonary hypertension can usually be differentiated by careful analysis of the signs and their etiological associations. Thus pulmonary artery syphilis, either in the form of Ayerza's disease, or pulmonary artery aneurysm,[5] pneumonoconiosis and sickle-cell anemia[6] can be eliminated probably with little difficulty. As a matter of fact, there have been so far two lesions which in our experience have been the source of error in diagnosis; these are (1) sinus of Valsalva aneurysm, particularly of the left anterior sinus, where the aneurysm presses on the pulmonary conus or artery, giving rise to signs of obstruction in the pulmonary circuit; and (2) mediastinitis. The former manifests itself by systolic murmur, thrill, and pulsation in the pulmonic area, but the diastolic shock is augmented by diastolic murmur; a positive Wassermann reaction is usually present, and the x-ray silhouette is decisive in the case of sinus of Valsalva aneurysm (of the left anterior sinus). Therefore, its globular bulge in the roentgenogram in the pulmonic area, its diastolic murmur, and positive serology serve to differentiate it from the lesion herein described. Such an aneurysm is usually intrapericardial, and while the peri-

cardium overlying the aneurysm is often inflamed and locally adherent, seldom is the heart itself attached to the surrounding structures. The second, more common, confusing condition that enters into the diagnostic problem, indurative mediastinitis, can apparently in certain cases give rise to almost identical physical signs. This lesion is not uncommon in connection with chronic pulmonary pleural tuberculosis, when it can develop as an extensive extrapericardial barrier, especially in the left hilar region. We have seen a tuberculous patient in whom there was marked systolic pulsation, followed by retraction in the pulmonic area in the entire absence, as shown later by necropsy, of intrapericardial adhesion. The mediastinal pleural tissue was extensively thickened, acting as a barrier to the expanding lung; the cushion effect of compensatory expansion of the lung during ventricular systole was then lost, permitting systolic retraction in the second and third left interspaces. A different mechanism occurring in pulmonary tuberculosis is the basis of the recent article by Geneverier and Descamps,[7] entitled "Pulmonary Arterial Syndrome in Sinistrocardia," in which physical signs, similar to those recorded in our patients, were ascribed to "extravascular stenosis of the pulmonary artery." These observers based their conclusions on a radiological study of tuberculous patients, in whom atelectasis of the left lung secondary to fibroid phthisis caused torsion and traction on the heart, pulling it to the left with subsequent "deformity" of the pulmonary artery. We believe that the fluoroscopic and clinical demonstration of a freely moving heart, the indubitable presence of pulmonary tuberculosis, the intense x-ray opacity of tuberculous mediastinitis in the left hilar area would in all probability aid in distinguishing the intrapericardial arterial constriction from obstruction, due to induration in the mediastinum or that possibly due to displacement of the heart.

The Effect of Constriction of the Pulmonary Artery on the Circulation.—Four of the six patients presenting this lesion succumbed relatively early in the course of their rheumatic disease, living at the most two or three years after the onset of the first severe attack. Death was due to recurrence of acute infection, and myocarditis must be accepted as the major factor in the final heart failure; mechanical obstructive heart failure appears to have been an incidental feature, overshadowed by the virulence of the acute infection. It is reasonable, however, to assume that even under these circumstances, compression of the pulmonary artery contributed to the defeat of the right ventricle.

Speculation as to what circulatory changes might have developed had these four patients survived is possibly answered by the histories of Cases 2 and 6. The former died after pregnancy from mechanical right heart failure without recurring infection. It is true that mitral stenosis was present, but the physical signs of pulmonary arterial

compression were also present; and to the extent that compression of the pulmonary artery is at least equal to the mitral lesion in the production of right heart failure, this case may be accepted as one illustrating the final effect of pericardial compression. In Case 6 the patient survived the acute phase of rheumatic disease for many years and did not, during the time of our observation, show any sign of recurring infection. In the absence of demonstrable serious valvular lesions, such as mitral stenosis or aortic regurgitation, this patient, we believe, illustrates even more fully than Patient 2 the evolution of mechanical right heart failure secondary to compression of the pulmonary artery by pericardial adhesions.

SUMMARY

Compression of the pulmonary artery by constricting pericardial adhesions is characterized by physical signs of (a) stenosis of the pulmonary artery; (b) pulmonary arterial hypertension of a proximal type; and (c) adhesive pericarditis.

The underlying pathological lesion in a group of six patients was rheumatic carditis.

While most of this group succumbed relatively early in the course of their rheumatic disease to recurrence of acute infection, in which the feature of mechanical obstructive heart failure was probably only incidental, or at best contributory to the final outcome, two cases were presented in which the adhesive pericarditis with compression of the pulmonary artery was a major factor in the development of cardiac failure.

The writer wishes to express his thanks to Dr. H. Schaeffer, Dr. F. Kalteyer, Dr. H. Jump, medical chiefs of the Philadelphia General Hospital, and to Dr. Bernard Kohn of the Jewish Hospital; to Dr. Gunn, Dr. Bevan, and Dr. Ahlfeldt, pathologists, for permission to use the clinical and pathological material; Dr. George Robson (deceased) performed the necropsy in Case 3.

REFERENCES

1. Churchill, E. D.: Decortication of the Heart (Delorme) for Adhesive Pericarditis, Arch. Surg. **19**: 1457, 1929.
2. Beck, C. S., and Griswold, R. A.: Pericardectomy in the Treatment of the Pick Syndrome: Experimental and Clinical Observation, Arch. Surg. **21**: 1064, 1930.
3. Moskovitz, E.: Hypertension of the Pulmonary Circulation, Am. J. M. Sc. **174**: 388, 1927.
4. Gouley, B. A., and Eiman, J.: The Pathology of Rheumatic Pneumonia, Am. J. M. Sc. **183**: 359, 1932.
5. Karsner, H. T.: Productive-Cicatricial Syphilitic Disease of the Pulmonary Artery, Arch. Int. Med. **51**: 367, 1933.
6. Yater, W. M., and Hansmann, G.: Sickle-Cell Anemia: A New Cause of Cor Pulmonale, Am. J. M. Sc. **191**: 474, 1936.
7. Geneverier, J., and Descamps, H.: Pulmonary Arterial Syndrome in Sinistrocardia, Presse méd. **43**: 1065, 1935.

CLINICAL OBSERVATIONS IN ERYTHROMELALGIA AND A METHOD FOR ITS SYMPTOMATIC RELIEF*

ISIDOR MUFSON, M.D.
NEW YORK, N. Y.

THE complaint "burning pain" in one or all extremities, induced or aggravated by warming or the dependency of a limb, and relieved by cooling or the elevation of a limb, is frequently encountered in vascular diseases. This symptom-complex has been named "erythromelalgia." Often, the underlying disease is so apparent, as in obliterative or vasospastic arterial diseases, or in inflammatory and allergic reactions, that this symptom-complex is passed over by the examiner. However, to the patient's comfort, it is very pertinent. Under the name "erythromelalgia" have been grouped those cases of peripheral vascular diseases, in which the presence of this type of pain is often associated with a rubor of the skin and a dilatation of the minute vessels of the skin. The causative agent is not apparent. First described by Weir Mitchell,[8] both Brown[2] and Lewis[6] have emphasized that erythromelalgia is but a symptom-complex. They also gave their criteria for its diagnosis. Lewis has further attempted to explain the mechanism of the pain, by assuming that there is a release of an histamine-like substance from the minute vessels, which, he suggests, are in a "susceptible state." Studies in two cases of erythromelalgia, to be reported here, it is believed, will show unusual underlying causes. Further, with the aid of observations on the blood pressures of the minute vessels, an attempt will be made to explain the mechanism of the pain. During the studies on the second case, we were able to devise a method for the symptomatic relief of the major complaint, pain.

METHODS

The minute vessels of the skin were studied through a binocular microscope with the forearm at the level of the heart. Blood pressure determinations were made on the minute vessels of the skin, near the cuticle margin of the nails by the indirect method.[3] The criteria used were the same as those in our previous work.[10] The pressure recorded is the figure most commonly recurring in twenty to thirty determinations. The final figures from the upper and lower extremes rarely vary more than 5 mm. Hg. The pressure was read on the mercurial manometer when the flow in the visualized capillary was fully reestablished while reducing the obstructing pressure of the closed capsule. The blood pressure in the venules was determined with the same apparatus.[10] Readings were

*From the Department of Medicine, College of Physicians and Surgeons, Columbia University and the Presbyterian Hospital.

made with the first return of color to the skin which had been blanched by the overlying closed capsule. Venous pressure was determined by the method of Moritz and von Tabora.[9] Skin temperatures were determined by means of a resistance thermometer (Leeds and Northrup).

CASE 1.—*Erythromelalgia Symptomatology in an Alcoholic Patient.*

A sixty-year-old man (Unit History No. 350653), divorced, for the past twenty years had drunk daily as much as a pint and a half of whisky. Six years before, a physician told him that he had alcoholic cirrhosis of the liver. He smoked ten cigarets a day. He had had gonococcus urethritis but no chancre. He was admitted to this hospital, complaining of increasing redness of the hands and enough pain in all fingers to render them useless. Nine months before, he first noted that his fingers were becoming awkward while playing cards, his favorite pastime. Four months later, he noted that the color of the skin of his fingers was becoming very red. They felt swollen and less supple. In the next two months the palms became involved. The lightest touch to his affected skin was unbearable. Warmth or hanging his hand down induced pain which could be relieved by cooling or elevation of his arm. He could not feed himself or smoke a cigaret, consequently he became extremely irritable and a "shut-in."

On examination, he appeared as an elderly lean male, chronically ill. His pupils reacted promptly; teeth were missing, nose, ears, and throat appeared normal. Thyroid was not enlarged. Heart and lungs showed no abnormality. His liver was 5 cm. below the costal margin, its surface was smooth but firm. The spleen was moderately enlarged. Rectal and genital examinations were negative. The neurological examination, which included an examination of his spinal fluid, disclosed no abnormality. Blood and spinal Wassermann reactions were negative. He had an eosinophilia of 6 per cent. His serum calcium was 10.8 mg. per 100 c.c. and his other blood constituents were within normal limits. His metabolic rate on several occasions was normal. X-ray examination disclosed no cervical ribs. The phalanges, however, showed an osteoporosis. His brachial blood pressure was 100/65 mm. Hg, and the antecubital venous pressure was 12 mm. water. His radial arteries felt sclerotic.

Both of his hands, especially his fingers and the palms, were bright red. There was no tinge of cyanosis; it rather suggested the color of freshly oxygenated blood. The skin was unbroken; there were neither vesicles nor ulceration, but there was some ironing out of the skin folds. Any attempt to touch his hands brought loud protests. Even after gaining his confidence during the weeks of hospital observation, he would resent the lightest stroking. The flexion of his fingers was also painful. When his arm was hung down over the side of the bed, his skin turned a deeper red, and pain soon set in. Elevating his arm relieved the pain in about a minute. A similar pain was induced when a blood pressure cuff was inflated around his arm. This could be relieved in several minutes by deflating it. Cooling the painful area by means of a spray of ethyl chloride gave him welcome relief, without any change in the depth of the color of his skin. His median nerve was blocked by the perineural infiltration of a 1 per cent solution of novocaine. The skin supplied by the nerve developed an increased surface temperature and its redness deepened.

The capillary microscope disclosed a marked alteration from the normal picture of the minute vessels of the skin. This was especially true of the venules. They were enormously dilated, with a diameter about five times the average. The blood in them was a bright red and accounted for the rubor of the skin. Capillary loops were few, but at the cuticle margin a complete row of them was visible. Their size was normal, and the diameter of their limbs, equal. The venules and the capillaries

contracted promptly when a drop of 1 to 1,000 solution of adrenalin was pinpricked into the epidermis. The skin became colorless. The even flow became slowed and interrupted.

Blood pressure readings of the minute vessels adjacent to the cuticle margin were made. These pressures varied directly with the changes in the temperature of the skin. These are recorded in Table I.

TABLE I

SKIN TEMP. ° C.	B. P. CAPILLARY MM. HG	B. P. VENULE MM. HG
27	34	28
34	45	40

Comment.—This case, on inspection, fitted into that group of cases which we usually catalogue as erythromelalgia, with the etiology usually undetermined. An analysis of the minute vessel studies in this case may enable one to associate the patient's alcoholic excesses with his vascular disturbance. The findings in the minute vessel studies were unusual. The dilatation that was anticipated was found only in the subpapillary venule plexus. The hypertension was localized in the minute vessels, the arterial and venous blood pressures being normal. With a rise in the temperature of the skin to almost blood temperature, the burning pain makes its appearance, and the blood pressures of the minute vessels rise to an extreme high. Lewis[6] assumes that the minute vessels must be in what he calls a "susceptible state" in order to give such severe pain in response to so mild a stimulus as a light stroking of the skin. Our observations lead us to feel that this pain response is due to the inordinate increase in blood pressure in the minute vessels of the skin. Dilatation per se of the minute vessels does not cause a blood pressure increase. Dilatation of the minute vessels is present with a low normal pressure in acrocyanosis, the spasm phase of Raynaud's disease, and in the cyanotic group of congenital heart disease without decompensation. Conversely, the hypertension found in nephritis is associated with vessels that are of a normal or constricted caliber. How, then, can the intrinsic hypertension of the minute vessels be accounted for? Alcohol is known to be toxic to the cytochrome of the tissue cells. Cyanide acts in the same way, more rapidly. An inactivation of cellular oxidation will follow the ingestion of a sufficient dosage. The tissue cell will not then be able to absorb its requirements in oxygen from the blood brought to it by its adjacent minute vessels.[5] This gas will then pass through without being absorbed. It then can be assumed that oxygen saturation will be about equal in the arterial and minute venous vessels. In cyanide poisoning, the skin of the patient has a bright arterial hue. One may assume that our patient has had such an inactivation of the cytochrome of the cells of his skin. His liver cells probably have experienced a similar change. The cellular anoxia enables the oxygen to reach the venule side in very high concentration. It was

found in a study of patients receiving oxygen by nasal catheter that an increase in its concentration caused a rise in the blood pressure of the capillary. In this patient, because of the cellular anoxia, a high oxygen concentration in the venule side of the minute vessels has resulted, and this in turn has stimulated an increase in the pressure of the minute vessels. The relationship of the osmotic pressure of the blood to the hydrostatic pressure of the minute vessels becomes disturbed. The exit of "pain substances" is hastened because the hydrostatic pressure is greater than the osmotic pressure. The distention, alone, of the minute vessels could be sufficient to cause the pain. This is often seen when a solution is given rapidly by vein with an overdistention of its lumen.

CASE 2.—A woman (Unit History No. 396258), aged forty-eight years, was admitted to the medical vascular clinic. For the past five years she had been under the care of various doctors in several of our hospitals. She first noticed a sense of pin-and-needle-like feelings in the first three digits of the left hand. A few weeks later there was severe pain in the left index finger. Not believing in medical care, she went to a cultist. Conditions grew worse, and after a year the pain became so intense that she consulted a physician. During this year she did not notice any loss of sensation or change in color of her skin. She received diathermy treatments and massage. Her tonsils were removed, and injections of several unknown drugs were given for several weeks. Diabetes was next discovered and controlled, but without affecting her pain. Two years before admission, she noticed that there was some blunting of her tactile sensation, though she was not entirely certain of this because of her pain, which was likely to be present at the time of her examinations. At this time she realized that the pain was relieved by cold and induced by warmth. After study in the Neurological Institute at this time the diagnosis was an osteoarthritis of the cervical spine and a provisional diagnosis of syringomyelia. A course of roentgen ray therapy to the cervical cord was given without any relief of her complaints. Next she developed a constricting pain in the middle of her left forearm and arm. Her friends also called her attention to the fact that her left eye appeared to be smaller than the right. She was followed in the neurological clinic, receiving sedatives and various forms of physical therapy. After two years she was referred to the medical clinic for an opinion. On her first visit here, she was discouraged in her failure to be helped and came only as a favor to the neurologists. The only additional finding was that the affected finger was insensitive to a deep pinprick. Her erythrocyte sedimentation rate was slightly elevated, 17 mm. per minute. X-ray studies failed to disclose a cervical rib. Her visual fields were normal. X-ray films of the teeth showed a mild infection which was treated. The basal metabolic rate was -13 per cent. The blood count was normal. Her glucose tolerance test showed a diabetic curve. A diabetic diet without insulin controlled the blood sugar within normal limits. At a medical conference additional hypotheses were suggested: first a vascular disturbance based on a cervical gliosis and, second, a thalamic syndrome involving the nucleus rubor which would explain the pains in the arms and leg.

The patient was then referred to the vascular clinic for further studies. She stressed the relationship of her pains to temperature. She preferred the cold to the warm weather. During the freezing weather, she walked with her affected hand exposed while the other was covered by a glove and a fur muff. At night, she had to keep an icebag on the painful hand in order to be able to fall asleep.

The skin of the affected finger was moderately atrophic, the skin markings being ironed out. The color of the skin was pinker here than that of the other hand. Capillaroscopy at the cuticle margin showed numerous capillaries. Their diameters were normal, with the blood flow occasionally showing an interrupted streaming. There was no dilatation of the subpapillary plexus.

When a blood pressure cuff, placed around the arm, was inflated to 120 mm. Hg, typical pain was induced in the left index finger. Examination of the capillaries under these conditions showed that a great increase in their number had resulted, the venules were dilated, and the blood flow stagnated.

The above procedure was repeated only after the affected finger had been subjected to a compression of 40 mm. Hg by means of an overlying capsule. No pain appeared in the finger when the pressure in the arm cuff was first raised to 120 mm. Hg, and then to 180 mm. Hg. When the finger compression was released, pain promptly appeared in the finger. Compressing the finger with the capsule, after the pain had already been induced by venous congestion, failed to give relief. The relationship of the occurrence of pain to changes in the temperature of the skin was observed. Simultaneously a record of the changes in the blood pressure of the minute vessels was made. These observations are recorded in Table II and are of great interest. The onset of pain when the temperature of the skin is close to blood temperature has been shown before. However, as in the previous case, it is now shown that a hypertension in the minute vessels occurs with the pain.

TABLE II

RELATIONSHIP OF PAIN TO CHANGES IN SKIN TEMPERATURE AND BLOOD PRESSURE OF MINUTE VESSELS

TIME	SPONTANEOUS PAIN				SKIN TEMPERATURE (° C.)				BLOOD PRESSURE (MM. HG)				REMARKS
									CAPILLARY		VENULE		
	R2	L2	R4	R4	R2	L2	R4	R4	R2	L2	R2	L2	
0.00	0	0	0	0	27.2	27.2	26.7	26.2	25	35	10	25	Left forearm immersed in hot water
0.05	0	0	0	0	32.5	32.5	32.0	32.0					
0.15	0	++	0	0	33.0	33.5	33.0	33.5	35	60	20	50	Capillary pulse present

Comment on Case 2.—From these observations, it appeared that the increase in skin temperature induced both an abnormal rise in the blood pressure of the minute vessels, and severe pains in the finger. Such a response is to be expected from a severe local trauma rather than such mild indirect warming of the skin. The minute vessels possess both constrictor and dilator fibers. The overdilatation could result from either group's being involved. With the constrictor pathways degenerated, the normal antagonism to dilatation may fail to exert its influence. Or it may be an exaggerated response by the dilator nerves to ordinary stimulation. In order to choose the mechanism for this response, we refer to the work of Meltzer and Auer,[7] who noted that adrenalin causes a greater constriction of the blood vessels of the ear when it is denervated than when its nerves are intact. Elliott[4] confirmed and extended these findings. He showed that the pilomotor mechanism is especially responsive to injected adrenalin after neurectomy. Others

have confirmed these findings and White has used this method to show why sympathectomy is a failure in Raynaud's disease. Meltzer and Auer[7] showed that this effect developed not immediately after denervation, but when degeneration was complete. Using these observations, one would be justified in concluding that if an exaggerated response to adrenalin be present, a degeneration of the vasoconstrictor fibers has taken place.

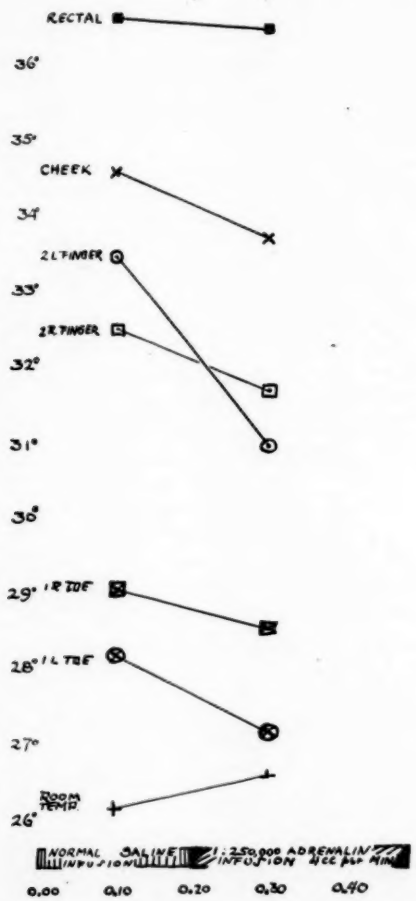

Fig. 1.—Case 2. Adrenalin response in erythromelalgia of left index finger.

Experimental Studies.—It was decided to test out the adrenalin sensitivity of the vessels. A solution of 1:250,000 was given intravenously at the rate of 4 c.c. per minute and frequent recordings of skin temperature were made. Vasospasm will result in a drop in the temperature of the skin. With the solution going in at the rate of 4 to 6 c.c. per minute, normal skin vessels will not become narrowed enough to give a drop in skin temperature. The results of this infusion test as given to this patient are recorded in Fig. 1. The temperature of the skin dropped most sharply in the painful areas of the skin.

As a corroboration of the value of this test, a definite case of syringomyelia with complete denervation of one side was given this infusion. He had a complete absence of sudomotor activity on his left side with the loss of pain and temperature sense. He showed a drop in the temperatures of the skin only in the right finger (Fig. 2). His vessels were sensitized to adrenalin because they had been denervated by the syringomyelic process.

It could therefore be concluded that vessels in the involved skin had been deprived of their vasoconstrictor nerve supply. The exact location where the interruption occurred is problematical. The sympathetic

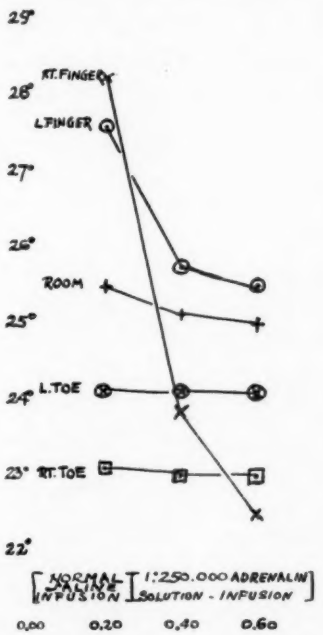

Fig. 2.—Adrenalin response in patient with syringomyelia affecting the right side.

fibers, according to Beattie and others,[1] pass at the dorsal levels through the vestibulospinal tract where they could be destroyed by a hydrops of the nearby spinal canal.

A week after this test had been performed, the patient returned for further studies. At this time, she enthusiastically stated that this was the first week in five years that she had been relieved of her pain and that she wanted more treatments. The infusion was repeated with similar changes in skin temperatures. The patient noted that when it was given rapidly she had greater relief. Normal saline given as a control had no effect. She did not mind the headache nor the palpitations which come with the higher rates of infusion because, as she stated, the relief was worth it. Her finger became pale and so did her face.

Her finger became mobile, and the hyperesthetic state was relieved. She was able to do her ironing. The relief, as was to be expected, lasted only for a few days after the infusion. She felt, however, that she would like to be that way all the time and wanted to come more often. At this time, a solution of adrenalin 1:100 appeared on the market. This was sprayed into the patient's nose and throat during ordinary respiration by means of a special nebulizer. The results were as satisfactory and almost as prompt as with the infusion of the dilute solution of adrenalin. She was told to use this at home, and she reported that she was able in this way to find relief at any time for her burning pain.

Since the patient had had many attempts to help her, and none had given her even temporary relief, it was felt that the response was genuine. Aside from the control infusion of normal saline, the following procedure was carried out to avoid the possibility that suggestion was

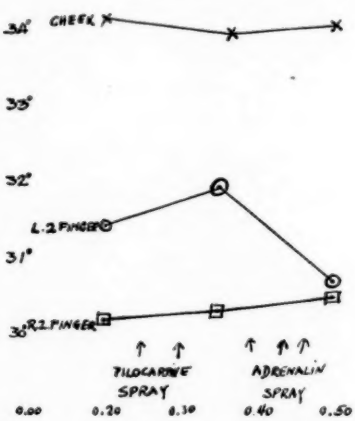

Fig. 3.—Case 2. A comparison of the skin temperatures after the spraying of pilocarpine and adrenalin into the nasopharynx.

the relief medium. One cubic centimeter of a solution of pilocarpine hydrochloride which contained 0.006 gm. of the drug was placed in the nebulizer without her knowledge. This was then sprayed into her nose and throat about fifteen times. After three minutes, she said that her pains were returning in a most severe form to her left hand. She became disheartened and thought that she had better go back to the infusion. She was then given the 1:100 solution of adrenalin by spray with prompt relief of the severe pain in the finger (Fig. 3). She felt more reassured when she was apprised of the experiment. She has since used the solution of adrenalin by inhalation, the total requirements per day varying directly with the temperature of her environment. She has been performing household duties of the so-called heavier type for the first time in five years. She is looking forward to a permanent cure, which, she has been told, is unfortunately not in sight.

SUMMARY

1. It has been reemphasized that erythromelalgia is a symptom-complex, dependent upon minute vessel changes, the etiology of which is not always readily apparent.

2. Capillary microscopy in the two cases studied has shown that the normal physiological response to warmth is disturbed and exaggerated, resulting in an intrinsic hypertension and dilatation of the minute vessels of the skin.

3. This exaggerated dilatation present in erythromelalgia has been shown to be the result of an absence of normal antagonistic vasoconstriction. The method was based on the work of Meltzer and Auer.

4. The use of this test led to the finding of a method for the alleviation of the most distressing pain. Relief of the pain was obtained by the use of adrenalin by infusion and inhalation.

REFERENCES

1. Beattie, J., Brow., G. R., and Long, C. N. H.: Physiological and Anatomical Evidence for the Existence of Nerve Tracts Connecting the Hypothalamus With Spinal Thalamic Sympathetic Centers, Proc. Roy. Soc. Series B **106**: 253, 1930.
2. Brown, G.: Erythromelalgia and Other Disturbances of the Extremities Accompanied by Vasodilatation and Burning, Am. J. M. Sc. **183**: 468, 1932.
3. Danzer, C. S., and Hooker, D. R.: Determination of the Capillary Blood Pressure in Man With the Capillary Tonometer, Am. J. Physiol. **52**: 136, 1920.
4. Elliott, T. R.: The Action of Adrenalin, J. Physiol. **32**: 401, 1905.
5. Keilin, D.: On Cytochrome, a Respiratory Pigment Common to Animals, Yeasts and Higher Plants, Proc. Roy. Soc. Series B **98**: 129, 1925.
6. Lewis, T.: Clinical Observations and Experiments Relative to Burning Pain in the Extremities and to So-Called "Erythromelalgia" in Particular, Clin. Sc. **1**: 175, 1933-34.
7. Meltzer, S. J., and Auer, C. M.: Studies in the "Paradoxical" Pupil Dilatation Caused by Adrenalin: I. The Effect of Subcutaneous Injections and Instillation of Adrenalin Upon Pupils of Rabbits, Am. J. Physiol. **11**: 28, 1904.
8. Mitchell, S. Weir: On a Rare Vasomotor Neurosis of the Extremities and on the Maladies With Which It May Be Confounded, Am. J. M. Sc. **76**: 17, 1878.
9. Moritz, F., and von Tabora, D.: Ueber eine Methode beim Menschen den Druck in oberflächlichen Venen exakt zu Bestimmen, Deutsches Arch. f. klin. Med. **98**: 475, 1910.
10. Mufson, I.: A Study of the Capillary Pressure in Nephritis and Hypertension, Am. J. M. Sc. **183**: 632, 1932.
11. White, J. C.: The Autonomic Nervous System, New York, 1935, Macmillan Company.

Department of Clinical Reports

PATENT DUCTUS BOTALLI WITH SUBACUTE BACTERIAL ENDOCARDITIS AND RECOVERY*

WILLIAM CHESTER, M.D.
MAMARONECK, N. Y.

THE following case is of unusual interest because it is the first recorded instance of recovery from subacute bacterial endocarditis in a patient with a patent ductus Botalli.

REPORT OF CASE

D. W., a woman aged twenty-nine years, was admitted to the Montefiore Hospital on Jan. 16, 1931. She had measles as a child. A tonsillectomy performed in 1929 was followed by a prolonged convalescence. She had had two pregnancies, and both children were living and well. In 1924, during her second pregnancy, a congenital heart lesion was detected.

In September, 1930, the patient was confined to bed because of a rise in temperature and weakness. Frequent chills and profuse sweats supervened, followed by anorexia, asthenia, and a rapid loss of weight. Soon she complained of a hacking, nonproductive cough, palpitation of the heart, shortness of breath, and precordial pain. In November, 1930, she was admitted to the Mount Sinai Hospital (New York City), where a diagnosis of patent ductus Botalli and subacute bacterial endocarditis *(Streptococcus viridans)* was made.

Examination on admission at the Montefiore Hospital revealed an emaciated woman weighing 89 pounds. Her face was flushed and the conjunctivae were pale. There was slight cervical lymphadenopathy. The apical beat of the heart was in the fifth intercostal space just outside the midclavicular line. The first sound over the pulmonic area was ringing in character, and the second sound was replaced by a continuous murmur. The heart rate averaged 120 beats per minute. The rhythm was regular, blood pressure 95/50. There were diminished resonance, bronchovesicular breathing and râles at the right base posteriorly. The spleen was firm, not tender; the edge was palpated 2 cm. below the costal margin. There was slight puffiness of the ankles. There was no clubbing of the fingers or toes.

The urine was negative. The blood count showed a hemoglobin content of 65 per cent; erythrocytes, 3,800,000; leucocytes, 10,800; polymorphonuclear leucocytes, 72 per cent; lymphocytes, 23 per cent; monocytes, 4 per cent; and basophiles, 1 per cent. A blood culture showed numerous colonies of *Streptococcus viridans.* The electrocardiogram showed a left axis deviation.

A roentgenogram of the chest showed that the right leaf of the diaphragm was high and moved very little with inspiration. There was marked pulmonary congestion of the central type. The heart was globular, and the left ventricle was rounded. The pulmonary artery and conus were prominent. The aortic arch was narrower than usual. The ascending limb of the aorta was well formed. There was some enlargement of the left auricle. Roentgenograms of the accessory nasal sinuses were negative. The diagnosis of patent ductus Botalli, subacute bacterial endocarditis *(Streptococcus viridans)* and infarcts of the spleen and lung (right lower lobe) were made.

*From the Medical Division of the Montefiore Hospital, Service of Dr. Leopold Lichtwitz.

Clinical Course.—During the patient's stay at the Montefiore Hospital, the clinical picture was that of severe sepsis. On Feb. 23, 1931, she experienced severe pain behind the right breast, aggravated by breathing, associated with dyspnea and cyanosis. Dullness and bronchovesicular breathing were present at the right base. A roentgenogram of the chest at that time revealed pleural thickening and pulmonary consolidation at the right base. Cough with slightly blood-tinged expectoration soon developed. The process was interpreted as pulmonary infarction. The signs at the right base persisted until the latter part of March and were accompanied by a cough with a yellowish expectoration, a low grade temperature, a rapid ventricular rate, and leucocytosis. On March 31, 1931, the patient had a chill, with a temperature of 104° F., and a ventricular rate of 118. She vomited and complained of increased sensitivity in the splenic region. From April 4 to Sept. 2, 1931, the septic course persisted. Frequent episodes of pain at the right base posteriorly and a productive cough were noted. On September 10, the patient was aphonic and showed a complete paralysis of the left vocal cord. The temperature was normal and the ventricular rate accelerated. A blood count at this time showed a hemoglobin content of 60 per cent; erythrocytes, 3,690,000; leucocytes, 6,500; polymorphonuclear leucocytes, 69 per cent; lymphocytes, 28 per cent; eosinophiles, 1 per cent; and myelocytes, 2 per cent.

On Oct. 7, 1931, the blood culture was sterile. The patient's condition was considerably improved. She had been afebrile since Sept. 30, 1931. On Oct. 14, 1931, marked depression, emotional instability, and auditory hallucinations were present. She insisted on going home and was discharged on Oct. 24, 1931, with the mental symptoms as noted. Her weight at this time was 59 pounds. The therapy during the patient's stay at the Montefiore Hospital consisted of the administration of supportive and symptomatic measures.

From Oct. 24, 1931, to February, 1932, the patient was confined to bed at her home. She became mentally clear and less anxious. During this entire period, she was afebrile and free from pulmonary and abdominal symptoms. Her appetite improved, and there was a rapid gain in weight. During the summer of 1932, she resumed her usual household activities and save for slight dyspnea on ascending a flight of stairs felt perfectly well. She commenced menstruating in October, 1932, after a period of amenorrhea of twenty-two months. Severe premenstrual and comenstral pain was present. Physical examination at this time revealed a well-nourished patient weighing 120 pounds, afebrile, and symptom free. The significant findings were the to-and-fro machinery-like murmur and systolic thrill in the second and third left intercostal spaces. The lungs were negative. The spleen could not be felt. There was no tenderness in the left upper quadrant. Fluoroscopy of the heart showed the same findings as noted while the patient was in the Montefiore Hospital.

The patient was again seen on March 18, 1934. Her weight at this time was 125 pounds, and her color was good. The menses had been regular since their onset in 1932, the dysmenorrhea persisting and frequently confining her to bed for a day or two. She performed her household duties without any difficulty. During this period she has had several mild upper respiratory infections, none of which confined her to bed. The heart findings were as noted on the previous examination. The lungs were negative. The abdomen, save for slight tenderness to pressure in the right lower quadrant, was negative.

DISCUSSION

Recovery from subacute bacterial endocarditis is not common. In the large series of patients with subacute bacterial endocarditis studied by Libman and Billings,[1] recovery occurred in from 2 to 3 per cent. Hem-

sted[2] described a complete recovery in a case of subacute bacterial endocarditis superimposed on a congenital defect of the right ventricle.

The unusual course of our patient's illness is remarkable and several points are worthy of emphasis: first, the question of the portal of entry of the *Streptococcus viridans*. In the 330 cases analyzed by Blumer,[3] a possible portal of entry is recorded in 17 per cent. That bacterial systemic infection may follow nose and throat operations is well known clinically. Nephritis and subacute endocarditis have been described complicating these procedures. In the subject of this report, a tonsillectomy with a protracted convalescence antedated the onset of the subacute endocarditis by a few months. It is worth stressing that these minor operations of the nose and throat should be performed during the quiescent stage of disease of the organs involved and that one should strictly consider the indications for operation in all cases and particularly in instances in which congenital or acquired disease of the heart is already present.

The occurrence of the transient left recurrent laryngeal palsy is interesting. This phenomenon was associated with an improvement in the patient's general condition and the commencement of the afebrile period which has persisted to the present time. The left laryngeal palsy present in the case reported by Schrotter and Mead[4] was found at necropsy to be due to the pressure of an enlarged patent ductus Botalli on the left recurrent laryngeal nerve.

The pathogenesis of the pulmonary infarction in this case deserves mention. In the absence of a venous source of emboli to the right side of the heart, one may postulate repeated pulmonary infarction of the right lung, due either to thromboses of the regional pulmonic vessels occurring in situ or to paradoxical emboli passing from the left heart to the right heart through the patent ductus Botalli and lodging in the pulmonary artery.

SUMMARY

Observations over a period of four years on a patient with a patent ductus Botalli and subacute bacterial endocarditis with recovery are presented.

REFERENCES

1. Libman and Billings: Quoted by Blumer.[3]
2. Hemsted, H.: A Recovery From Infectious Endocarditis (Streptococcal), Lancet 1: 10, 1913.
3. Blumer, G.: Subacute Bacterial Endocarditis, Medicine 2: 105, 1923.
4. Schrotter and Mead: Quoted by Abbott, Maude: Congenital Heart Disease, Osler and McRae—Modern Medicine, Vol. 4, Philadelphia, 1915, Lea & Febiger, p. 418.

Department of Reviews and Abstracts

Selected Abstracts

Selected Communications Presented at the Society for Digestive and Metabolic Disorders held in Berlin from July 27 to 31, 1936. (Adapted from the report in the Ztschr. f. Kreislaufforsch., pp. 846 to 850.)

1. Cassisnis (Rome): New Heart Measurements.

Three dimensional measurements made with x-ray show that the heart is definitely bigger in athletes than in nonathletes.

2. Bohnenkamp (Freiburg): Metabolism and Limits of Work of the Heart.

The author reviews the subject. He points out that the heart differs from skeletal muscle in chemical composition. It has more calcium, chlorine, phosphatides, and less potassium and creatin. It has no adenosine phosphoric acid. It depends on a plentiful oxygen supply, and it consumes 4 per cent of the total oxygen consumed by the body. Its oxygen consumption depends on the heart rate and the minute volume output. The oxygen consumption of each beat depends on the diastolic size of the heart. A rapid heart is a less efficient machine than a slow one. In trained individuals, the heart does not speed up as much as in the untrained; hence it is more efficient. At rates above 180 or 200 an inadequacy of coronary flow develops; the heart dilates so that its oxygen consumption increases and it becomes more inefficient. This insufficiency is later contributed to by the development of cardiac irregularities.

3. Knoll (Hamburg): Cardiac Work and Electrocardiograms.

He found a notching of QRS and depression of the S-T segment following severe exercise in normal athletes.

4. Hochrein (Leipzig) confirmed the preceding observations. At times the electrocardiographic picture may resemble that seen in coronary disease. He found that straining causes a sudden outpouring of blood from the lungs into the left ventricle and thereby leads to left axis shift. Later right axis shift develops because the right ventricle works against an increased resistance.

5. Thörner (Bonn): New Observations on Training of Dogs.

Dogs were trained to run on a treadmill. The hearts of those animals running a long distance increased in size when viewed under x-ray.

6. Matteff (Sophia): Orthostatic Circulatory Collapse in Man Following Exercise.

This circulatory collapse is due to gravity shock. The blood pressure sinks to 35 mm. Hg. It can be relieved by placing the individual in a horizontal position and putting elastic bandages on the legs. Hence, it is due to "bleeding into muscle vessels" which follows the stoppage of the muscle pumps.

7. Rein (Göttingen): The Meaning of Metabolism for the Heart and Respiration.

His own methods of measuring the blood flow in intact animals have shown that adjustments of the heart and respiration to metabolic needs are peripheral in origin. The first is the adjustment of the blood flow in the muscle to its need. The activity of circulation and respiration increases two seconds after the onset of effort. This early increase must be reflex in origin since it fails when the muscles are denervated. Carbon dioxide is the other stimulus which operates on the vasomotor, cardiac and respiratory centers, and adrenalinemia is a supplementary mechanism.

8. Broemser (Munich) emphasized the value of the venous valves in aiding onward movement of the blood.

9. Kroetz (Altona): Circulatory and Chemical Blood Regulation During and After Exercise.

Training tends to improve the distribution of blood so that less goes to inactive organs. This acts to lessen the amount of augmentation of minute volume flow required by the heart. There is a linear correlation between flow and exercise, and this correlation is characteristic for each individual and for each type of exercise. The relative acidity of blood during exercise leads not only to a local dilatation of blood vessels but also to dilatation in the lung and thereby aids oxygen exchange. The acidity also leads to dilatation of the coronary arteries, and the increased lactic acid content of the blood makes available a source of nourishment for the heart which keeps down its oxygen consumption. In addition to acidity in general, carbon dioxide acts as a specific stimulant.

L. N. K.

Selected Communications Presented at the Society of German Biologists and Physicians held in Dresden from Sept. 20 to 23, 1936. (Adapted from the report in the Ztschr. f. Kreislaufforsch., pp. 851 to 861.)

1. F. Volhard (Frankfurt): Value of Eyeground Examination in Hypertension and Renal Disease.

The author found that uremic amaurosis, uremic spasm, and albuminuric retinitis can occur without appreciable decrease in kidney function. Amaurosis and retinitis are evidence of a deficient cerebral blood supply, and the arterial spasm is evidence of an increased intracranial pressure. Contraction of the small vessels in the eyegrounds in hypertension is a sign of generalized constrictions of these vessels throughout the body, including those of the kidney. It is not related to blood cholesterol content. Albuminuric retinitis (also known as ischemic or angiospastic retinitis) is a danger sign, indicating similar states in vital organs elsewhere.

A drop in blood pressure is an important therapeutic procedure in nephritis since a rise in blood pressure is "a misfortune for the kidney." The elevated pressure in nephritis is not nervous in origin but is due to some chemical substance's being carried away from the kidney by the blood. The kidney is the only organ besides the adrenal and pituitary from which such vasoactive substances seemingly are liberated.

Retinitis occurs in "pale" hypertension and usually not in "red" (essential) hypertension. When it occurs in essential hypertension, it is evidence of the onset of malignant nephrosclerosis.

2. **Thiel (Frankfurt): The Significance of Eyeground Examination in the Diagnosis and Differential Diagnosis of Hypertension and Kidney Disease.**

In essential (''red'') hypertension of Volhard only the systolic pressure is elevated, and there are no renal damage and no eyeground changes. In fact, the retinal vessels are dilated. The appearance of sclerosis is indicated by whitish gray streaks along the vessels and small discrete hemorrhages. Later arteriosclerotic retinitis develops with retinal hemorrhages which follow thrombotic arterial closures or venous occlusions. As the hemorrhages disappear, they give rise to white speckling which appears and disappears. Papilledema and vascular spasm with ''silver wire'' vessels in the eyegrounds is the evidence that the hypertension has changed from the ''red'' to the ''pale'' form. At this stage yellowish white spots appear, and the picture is that of angiospastic retinitis.

3. **Siebeck (Berlin),** in discussing the circulatory complications of hyperthyroidism, emphasized the value of potassium iodide (0.5 gm. three times a day) given together with digipurat (2 c.c. intravenously two to three times a day). The arrhythmias and tachycardias of hyperthyroid states are best treated with quinidine.

4. **Bansi (Berlin)** emphasized the frequent occurrence of hypertension in hyperthyroid disease. Tachycardia in hyperthyroid states, when the only abnormality, is not evidence of circulatory insufficiency. Arrhythmias and paroxysmal tachycardia, on the contrary, are indications for surgical intervention. Thyrotoxic myocarditis is difficult to diagnose clinically.

5. **Olivet (Berlin): Arteriolosclerotic Hypertension (''Pale'' Hypertension).**

The prognosis of this form of hypertension is from three to six years. A high diastolic pressure is a sign of bad omen. Headache, albuminuria, polyuria occur early in the disease, and eyeground changes are prominent. Late in the disease changes in kidney function become apparent.

6. **Böhme (Rostock)** reported the findings in two cases obtained by roentgenkymography. Kymography of a thirty-two-year-old man who had suffered from pulmonary hemorrhages since the age of eight showed in the left hilus a walnut-sized shadow which had arterial pulsations. This tumor was connected to the aorta. A systolic murmur was audible over the chest in the region. These findings led to the diagnosis of a patent ductus arteriosus with saccular aneurysm of the pulmonary artery. On deep inspiration this aneurysm increased in size and the arterial pressure fell 20 mm. Hg. This aneurysm caused venous stasis and bronchial varicosities by compression of the hilus; and the latter were the source of the pulmonary hemorrhages. Kymography of a twenty-year-old boy with cardiac dilatation following paratyphoid fever showed marked pulsations of the upper third of the left heart border with the pulsations in the lower two-thirds moving in the opposite direction. In this case there was an inspiratory elevation of the cardiac apex which the author considers a sign of cardiac dilatation.

He then reported some observations on animals in which x-ray opaque substances were injected into the circulation. In this way he noted marked fluoroscopic evidence of a systolic suction by the ventricles, which caused the auricles to fill at this time. In animals with damaged circulation or cardiac dilatation he found that this suction action diminished or was absent. In determining the work of the heart, this systolic suction must be included in the calculations.

7. Kroetz (Altona): Peripheral Veins in Rheumatic Disease.

The author reports the presence of venous sacculations and venous enlargement in the lower extremities during rheumatic disease. These disappear after the rheumatic fever has healed. He used infra red photographs to study these vessels or employed ruby glass through which he could view the leg. These venous enlargements may be inflammatory or the reaction to the products released in the inflamed joints.

8. Vodel (Berlin) advocated the use of breathing exercises to lower blood pressure in hypertension. The breathing was the deep abdominal type used against light resistance. This was carried out two or three times a week, each period being for twenty to twenty-five minutes.

L. N. K.

Selected Communications Presented at the German Physiological Society held in Giessen and Bad Nauheim from Aug. 30 to Sept. 2, 1936. (Adapted from the report in Ztschr. f. Kreislaufforsch., pp. 816 to 820.)

1. K. Matthes (Leipzig): Studies on Oxygen Saturation of Arterial Blood in Man.

The author determined oxygen saturation of arterial blood within the ear and finger by his own method and compared it with alveolar oxygen tension. He found that a definite difference existed between the oxygen tension in the blood and the alveoli. He used this method also to determine the blood velocity in terms of circulation time.

2. W. Springorum (Göttingen) and D. Centenera (Madrid): Blood Flow of Both Kidneys Studied with Rein Stromuhr.

The flow is not proportional on the two sides, and differences of as much as 100 per cent occur. These differences vary from time to time and are not related to diuresis. Vasoconstrictor substances do not affect vessels of both kidneys equally.

3. F. Palme (Bad Nauheim): Concerning the Chemical Receptors of the Carotid Sinus.

Adrenalin in some animal species causes a long lasting blood pressure drop when applied to the carotid sinus. This is due to stimulation of the sinus nerve and seems to depend on the amount of chromaffin cells in the paraganglion caroticum. This and other evidence suggests that the chromaffin material is a hormonal regulator of the carotid sinus. The author believes this will explain many observations previously attributed to chemical receptors.

4. E. Holzlöhner (Kiel): Systolic Suction of the Human Heart.

The cardiopneumogram of man is a measure at any moment of the difference between the amount of blood discharge from the thoracic arteries and the amount of blood entering the thorax via the veins. The smallness of the change in the pneumogram occurring during systole indicates that a suction action of the contracting ventricle brings into the chest an amount of blood almost equal to the amount discharged from it in systole.

5. O. F. Ranke (Berlin): Importance of Position on the Ability to Withstand Acceleration.

When acceleration exceeds 7 gm. in the lower limbs, petechia occurred. (This acceleration was apparently obtained by the author by centrifugal force, but this is not so stated in the abstract from which this report is made.)

6. E. Schütz and B. Lueken (Berlin): Changes in Irritability of Heart Following Systole.

A method of stimulating the heart at the end of its monophasic action curve with rectilinear electrical impulse of very short duration is described. The threshold of irritability falls rapidly at the end of the monophasic curve and reaches normal in about one-tenth of the time occupied by the monophasic curve. Potassium lengthens the refractory phase, and calcium shortens it. A similar antagonism is demonstrated between adrenalin and acetylcholine. Wherever a marked lengthening of refractory phase occurred, direct leads showed an extremely small and short action current.

7. E. A. Müller (Munster): Heart Work and Heart Volume.

At constant minute volume output an increase of arterial pressure in the pulmonary vessels increases the size of the right heart five to seven times more than the increase produced in the size of the left heart by a similar rise in aortic pressure. It is not possible to study the action of an increased minute volume at constant resistance in the heart-lung preparation since the increased minute volume causes both the right auricular and pulmonary pressures to rise.

8. Kahlson (Lund) and O. Mertens (Göttingen): The Cardiac Minute Volume in the Intact Animal Following Adrenalin.

The authors find that the minute output of the heart never increases and in many cases actually decreases to a slight or marked extent following adrenalin injection. In the rest it is unchanged. The flow in a limb decreases by 70 per cent during the eight minutes of adrenalin action. This is usually more or less compensated for by the splanchnic area.

9. H. Gerstner (Leipzig): The Problem of Blood Pressure Rise Following a Strong Electrical Current.

Both the abdominal and arterial blood pressures rise when a strong electrical current is passed through an animal.

L. N. K.

Springorum, W.: The Reactions of the Vessels of the Skin to Active Principles of the Body. Arch. f. d. ges. Physiol. **238**: 353, 1936.

The author employed Rein's thermostromuhr for measuring the blood flow in small arteries known to supply, and small veins known to drain, only skin. The animals used were dogs. Two sites were selected as most convenient: a small artery and vein (1) serving the skin of the ear and (2) those serving an area of the hip and thigh. Simultaneous records were in this way obtained of the flow of blood in a small artery supplying skin, the small vein draining that particular region, and the arterial pressure in the carotid or femoral artery.

Small amounts of adrenalin caused a prompt decrease in blood flow through the artery and a somewhat slower return to the normal rate. Two types of reaction were observed in the veins: one in which the change in rate of flow followed that in the artery almost simultaneously and one in which a small increase accompanied the decrease in the artery and then a delayed decrease which was considerably slower than that of the artery in returning to normal. The latter reaction is of considerable interest, for in this reaction lies the explanation of mobilization of a not inconsiderable amount of blood ordinarily stored in the skin. Figures for the relative frequency of the two types were not given. The flow of blood into the skin through

the artery decreases while that flowing out increases. This dissimilarity in flow may persist for as long as a minute. The author states that he wishes to emphasize the fact that the type of venous flow varies not with the site chosen for study but with the individual animal.

Histamine evokes a sharp *increase* in flow through both the artery and vein, almost simultaneous with the fall in arterial pressure. The venous response may be delayed, thus providing for *storage* of blood in the skin. It was also observed that if the dose of histamine was larger, the curve of increase of peripheral flow might be temporarily interrupted only to continue on to its peak simultaneously, with reestablishment of arterial pressure. This phenomenon appeared to be plainly a passive one to the author and might be capable of explaining variation in the published results. The results obtained with acetylcholine were for the most part very similar to those obtained with histamine, but were, perhaps, more pronounced. The study demonstrates clearly the occurrence of withdrawal or admission of blood to the depots in the skin. In passing, the author mentions the fact that the skin is apparently ten to fifteen times as sensitive to adrenalin as the kidney.

J. M. S.

Bärtschi, W.: The Reaction of Coronary Arteries to Acetylcholine. Arch. f. d. ges. Physiol. **238:** 296, 1936.

Because of confusion over the question of the reaction of the coronary arteries to acetylcholine, the literature of which the author briefly reviews, Bärtschi thought that it was worth while to test in a standard manner a rather large number of specimens. Twenty-nine preparations of ox-heart coronary arteries were tested one hundred and eleven times. The almost invariable result was contraction. In one preparation contraction was obtained eleven successive times without diminution. It followed as great a dilution as one part in 25 million in one instance; sometimes as much as one part in 500,000 was needed. Atropine abolished the reaction, adrenalin reversed it; that is to say, adrenalin was followed by dilatation. The experiments were carried out on excised rings of arteries, 2 mm. wide, obtained from animals one and a half to two and a half years old, at times varying from one hour to three days after slaughter. That atropine abolished the reaction would appear to obviate the objection to the use of excised rings.

J. M. S.

Dragstedt, Carl A., and Mead, Franklin B.: A Pharmacologic Study of the Toxemia Theory of Surgical Shock. J. A. M. A. **108:** 95, 1937.

The abrupt vasomotor symptoms of anaphylactic shock may be duplicated by rapid intravenous injection of a large dose of histamine. In each instance the presence of a vasodepressor, smooth muscle stimulating substance which is apparently histamine, can be detected by the usual biological assay of heparinized blood plasma or thoracic duct lymph. In nine experiments on dogs in which the surgical shock was produced by traumatization of one or both hind legs or by traumatization of the extruded intestine, or a combination of these procedures, no physiologically active substance could be found in the blood or lymph.

In an attempt to duplicate the gradually progressive blood pressure fall of surgical shock in order to eliminate the objection that histamine might not be detected because it is soon inactivated, the authors used slow continuous intravenous injection of varying concentrations of histamine without success in exact reproduction of surgical shock.

Four twin experiments were performed using two dogs each. In the one dog surgical shock was produced, in the other shock was produced by histamine sub-

cutaneously. Samples of blood and lymph were taken and tested simultaneously. Uniformly, blood samples in surgical shock were negative, while in the same amount of shock by histamine the samples were positive.

L. S.

Brouha, L., Cannon, W. B., and Dill, D. B.: The Heart Rate of the Sympathectomized Dog in Rest and Exercise. J. Physiol. 87: 345, 1936.

The factors which determine the acceleration of the heart rate as a result of exercise have been studied in many experiments. In order to obtain additional information concerning these factors, a series of experiments has been performed on totally sympathectomized dogs. A standard form of exercise on a motor-driven treadmill, running at different speeds for different periods of time, was used to test the behavior of the dogs. From these experiments one can conclude that the cardiac rhythm of the inactive sympathectomized dog is less than that of the normal animal. However, emotional excitement produces definite cardiac acceleration, and on exercise there is an increase in heart rate which is about 30 to 40 per cent below that of the normal dog. The general behavior in dogs is quite different from that of sympathectomized cats. The capacity to withstand intense exercise is not diminished in the sympathectomized dog, but because of lack of training there is a lessened capacity for prolonged exercise for from six to eight weeks following sympathectomy. This differs somewhat from the results obtained in a similar experiment by Samaan, who found that his sympathectomized dogs had an increased capacity for work despite the fact that their heart rates were only two-fifths the normal maximum. Cardiac acceleration after sympathectomy is not due to a rise in body temperature nor to muscular metabolites, secreted adrenalin, or sympathin, but is probably due to a reduction in the tonicity of the cardioinhibitors of the vagi and an increase in the tonicity of the vagal cardioaccelerators.

E. A. H.

Kreuzfuchs, S.: Occult-Pulmonary Cardiopathy. Ztschr. f. Kreislaufforsch. 28: 841, 1936.

The author describes lung conditions which displace the trachea in the x-ray picture and change the aortic shadow. The symptoms in such cases are not to be considered cardiac in origin nor should they be described as neurotic manifestations. They are evidence of the pulmonary involvement.

L. N. K.

Eldblom, L. E.: Investigations of the Difference in Skin Temperatures Between the Lower Extremities in Unilateral Sciatica. Acta med. Scandinav. Suppl. 78, Report of 17th Scandinavian Congress of Medicine, June, 1935, p. 834.

The results of studies on 43 normal and 57 individuals with sciatica are given. The method of measuring what the author speaks of in the title as "skin temperatures" and usually in the text as "heat-transmitting capacity" is of considerable interest. Cylinders lined with cloth are placed about the thighs, the ends being closed by boards with holes in them to fit the leg so lightly that disturbance of the circulation does not occur. The bulb of a mercurial thermometer is thrust through a snugly fitting hole into this rough calorimeter, leaving the scale, reading in 0.1° C., outside. The cylinders are the same size. The two pairs of boards chosen to close the upper and lower ends have apertures of the same size, and so, whether or not the two legs are of the same size, when the cylinder and boards are pushed far enough up the thigh for the apertures to fit snugly, approximately equal areas of skin are included in the two calorimeters. The thermometers are then read until

their recorded temperature has become constant, which takes place within from forty-five to seventy-five minutes. Obviously the temperature in the cylinders bears some relation to the rate of heat production of the enclosed leg and to the rate of heat lost to the room. If the latter is constant, the temperature increases in some fashion with increase in production of heat by the tissue enclosed. The author states that "actual 'absolute' temperature of the skin is at most only an abstract idea," and that relative measurements therefore often furnish adequate data for comparing blood flow.

In 43 normal individuals, the final differences in temperature which were established within the cylinders on the two thighs were 0.2° C. in 7, 0.1° C. in 16, less than 0.1° C. in 3, and 0.0° C. in 17. In 57 individuals suffering from sciatica the calorimeter on the affected leg was less than the normal by from 0.5 to 0.9° C. in 15 cases, by 0.4 in 5 cases, and by 0.3 in 14 cases. That is to say, 34 cases showed differences greater than normal. Ten were borderline cases (0.2° C. difference always, however, lower on the affected side) 8 were normal, and 5 showed temperatures higher on the affected than on the normal leg. He states that all of the last groups had been treated. Eleven cases were studied during recovery, and in each a tendency to increase in temperature with respect to the normal side was observed.

In one experiment a normal individual was subjected to rather excruciating pain by placement of paper clips and "Paens" forceps on the skin of the foot and thigh of one leg. The position of the clips was frequently changed. Contrary to most observations of surface temperature in pain, a rise in heat-transmitting ability occurred not only in the injured, but also in the opposite leg and to the same degree. This suggests that the low temperature usually found in the sciatic limb is not a pain reflex.

Concluding from these observations that many cases of sciatica are associated with, if not due to, a lowered blood supply the author proceeded to treat them with caffeine, which he has previously demonstrated to be a vasodilator of skin vessels, and with "fever treatment" by injecting suspensions of killed colon bacilli. For both of these forms of treatment he claims excellent results although details are not given. With the onset of fever he observes that the heat transmitting capacity of both legs rises and the pain disappears, the affected one lagging behind at first but gradually attaining the same capacity as the normal leg.

J. M. S.

Kenenhof, W. T., and Kohl, H.: Contributions to the Physiology of Age: IX. Chemical and Histological Studies Upon the Aorta of the Horse. Ztschr. f. d. ges. exper. Med. **99:** 43, 1936.

The authors have undertaken the present study as a sequel to the studies of Bürger and Schlomka dealing with chemical changes in tissues with age in order to furnish additional evidence concerning purely physiological changes with age. The horse was chosen for study because the cow and ox, studied by Gerritzen, are usually slaughtered before the age of fifteen years.

The aortas were obtained from 69 horses, 20 from 1 to 10, 29 from 11 to 20, and 20 from 21 to 36 years old. The animals had been for the most part engaged in farm work and fed on oats, hay, chopped straw, and bran. The thickness of the wall and content of moisture, nitrogen, cholesterol, and calcium were studied. Histological sections were also made.

The thickness of the wall of the arch increased from 4.75 to 6 mm. (average of the first and third decades), but at the caudal end no increase occurred. The dry weight in grams per cent of fresh tissue increased regularly for each decade, the first 22.56 per cent, the second 25.15 per cent, the third 26.30 per cent, but the

nitrogen content was, interestingly enough, greatest in the second decade, 4.23 gm. per cent of fresh tissue (first decade, 3.88, and third, 3.93 gm. per cent). It follows obviously that the increase of dry weight did not represent merely a uniform loss of water. This conclusion was borne out by the fact that cholesterol and calcium contents increased markedly and were found to be respectively, in the first decade 144.4 and 12.80, in the second, 202.9 and 20.58, and in the third 240.3 and 27.2 mg. per cent.

Histological changes were most striking in the media. Two microscopic sections, one from the aorta of a six-year-old, and one from a twenty-six-year-old horse, are reproduced. The essential changes were decrease in the number and concentration of elastic fibers and nuclei and deposition of an indeterminate gelatinous substance which is, as deduced from staining reactions, not amyloid, hyalin, or glycogen. The substance was found to stain specifically with cresyl violet.

Because of the nature of the diet of these animals, the authors believe that the changes observed were not related to it and that they have, therefore, to do only with physiological aging. They express the opinion that because of the work of Anitschow and subsequent workers entirely too much emphasis has been placed upon the influence of diets rich in ergosterol and cholesterol which were, apparently, conspicuous by their absence in the diet of the horse, and upon the use of nicotine and alcohol which the horses obviously did not use.

One criticism of the criteria used for estimation of age, namely, condition of the teeth, seems, however, to merit attention. It is conceivable that the physiological age of the teeth might parallel the physiological age (as described) of the aorta rather than the chronological age of the animal.

J. M. S.

Weiss, Soma, Wilkins, Robert W., and Haynes, Florence W.: The Nature of Circulatory Collapse Induced by Sodium Nitrite. J. Clin. Investigation **16**: 73, 1937.

Sodium nitrite, which in the prone normal subject will produce slight or no circulatory changes, will lead in the upright patient to progressive vasomotor collapse, often terminating in syncope. A study of seven normal adults showed that after administration of sodium nitrite the upright position produced restlessness, yawning, perspiration, cyanosis, ashen color, drowsiness, dilated pupils, and syncope. The systolic blood pressure fell; the diastolic blood pressure was sustained; and the venous pressure fell rapidly to a level below the hydrostatic level of the right auricle; tachycardia was present until bradycardia appeared just before syncope; and the maximal blood flow through the hand was moderately decreased until just before syncope when it decreased to zero. The blood flow to the legs decreased in the upright position before and after administration of sodium nitrite. Skin temperatures and electrocardiograms showed no remarkable changes.

The vasomotor collapse produced by sodium nitrite is essentially due to a disproportion between circulating blood volume and the volume of the peripheral vascular bed, caused by a peripheral pooling of blood.

L. S.

Wilkins, Robert W., Haynes, Florence W., and Weiss, Soma: The Rôle of the Venous System in Circulatory Collapse Induced by Sodium Nitrite. J. Clin. Investigation **16**: 85, 1937.

Using the *height* of the plethysmographic tracings as an index of decreased resistance of the "venous" vessels to stretch, and the *steepness* of the curves obtained as an index of arteriolar resistance to blood flow, the authors found a definite decrease in the "venous" tone after administration of sodium nitrite; even in the simul-

taneous presence of an increase in the resistance offered by the arterioles to the flow of blood. There was definite decrease in "venous tone" in four of five subjects tested at 37.5° C. The variable response of the hand at 32° C. became marked response in the presence of reflex vasodilatation produced by placing the opposite hand in water at 45° C. Decrease in resistance to stretch in the veins following administration of sodium nitrite results in an excessive dilatation of these vessels under the additional stress of the hydrostatic pressure of blood when the subject is in the upright position; this results in a peripheral pooling of blood.

These observations demonstrate a blood depot in addition to that in the splanchnic area. Certain types of collapse may be attributable to this peripheral depot.

L. S.

David, F., and Siedek, H.: A Bloodless Method for Measuring Pressure in the Pulmonary Artery. Ztschr. f. d. ges. exper. Med. **100**: 54, 1936.

The method was suggested to the authors by the observation during bronchoscopy that a certain portion of the wall of the right bronchus pulsated synchronously with the heart and by the fact that anatomically this portion lies almost against the pulmonary artery. The procedure is to place a small rubber balloon in the bronchus at the point which pulsates, to connect it by a rubber tube to a mercury manometer, a Frank capsule, a Broemser glass membrane manometer, a slow release valve, and a pressure pump. The balloon is then blown up to a pressure exceeding that existing in the artery and allowed to fall slowly. The Frank capsule records the pulsation, the glass membrane manometer the level of pressure (calibrated by the mercury manometer) optically upon photographic paper. The point at which the ordinate passing through the region of maximum pulsation as registered by the Frank capsule cuts the simultaneous record of pressure in the balloon is taken as the pressure in the pulmonary artery.

The four records given as samples of some 35 or 40 experiments on dog and man are far from decisive not only as to where oscillation begins and ends, but even as to where maximum oscillation occurs. Eight comparisons of this method in dogs with direct measurements agree, however, within 10 per cent. The range of pressures found to exist in the pulmonary artery was from 18 to 40 mm. Hg for both dog and man.

The ingeniousness of the method is admitted, but until clearer oscillatory records can be obtained enabling one to estimate systolic and diastolic levels, or at least a clear-cut mean pressure, the method would not appear to be useful. One must recall also that the anatomical proximity of the pulmonary artery to the bronchus is the only evidence offered that what is being measured is really pulmonary arterial pressure.

J. M. S.

Looney, J. M., and Jellinek, E. M.: The Oxygen and Carbon Dioxide Content of the Arterial and Venous Blood of Normal Subjects. Am. J. Physiol. **118**: 225, 1937.

A study has been made of the venous blood oxygen and carbon dioxide in 67 normal subjects and of the arterial blood in 29 normal subjects. The levels of these gases in both arterial and venous blood show considerable variation in the same individual at different times. The normal mean value of venous oxygen is lower and the mean value of carbon dioxide is higher than the values commonly accepted.

These differences are thought to be due to too much reliance on oil to protect the blood gases from exchange with the atmosphere. No significant correlation was found between the levels of arterial and venous oxygen or carbon dioxide.

E. A. H.

Kohan, B., and Hoffmann, J.: Electrocardiographic Observations in Malaria. Ztschr. f. Kreislaufforsch. **28**: 643, 1936.

There is no characteristic electrocardiographic abnormality in malaria, and there is no relation between the amount of abnormality and the severity of the malaria. A common finding in such cases was a transitory prolongation of A-V conduction during the febrile stage of the cycle. In addition in the febrile stage, transitory changes occurred in the P- and T-waves accompanied by a lengthening of the duration of systole.

L. N. K.

Gotsev, T., Lucken, B., and Simmendinger, W.: The Influence of the Splanchnic Region upon the Systemic Blood Pressure. Ztschr. f. d. ges. exper. Med. **100**: 81, 1936.

A series of elaborate and yet, in certain ways, rather crude experiments are described in which various portions of the circulatory system were excluded by ligature from participation in vascular reactions to various drugs. The effects of adrenalin, nicotine, histamine, and acetylcholine were studied, first with the circulation intact; second, before and after extirpation of the splanchnic region; third, after various regions such as the head, forelegs, or hindlegs had been excluded; and fourth, when only the splanchnic region remained in the circulation. Oncometers were usually placed about a portion of the small intestine and occasionally about the spleen. In another series of experiments the outflow from the portal vein was measured. The arterial pressure was always recorded, usually by connecting an artery to a mercury manometer. There is a detailed account of the results in each group of experiments and many reproductions of smoked drum records.

The description of the results for the various groups of experiments and the conclusions drawn therefrom are, to the reviewer, confusing and even, in some instances, contradictory. By the described methods, the following reactions of the intestinal vessels were found to exist: 1. After adrenalin and nicotine, vasoconstriction occurred, followed, as previously described by the authors, by vasodilation. The latter reaction is by the present work proved to be passive, i.e., occurs because the blood pressure remains elevated after the peripheral vessels have returned to normal caliber. An elaborate and perhaps misleading method of calculating peripheral resistance (ratio of change in pressure to change in venous outflow per unit of time) is used to substantiate this argument. 2. Acetylcholine gives rise to vasoconstriction in the splanchnic region followed often by vasodilation. Of interest with regard to this conclusion is a record in which a rise of blood pressure and a simultaneous constriction of the vessels of the small intestine follows injection of acetylcholine when the splanchnic region only is in the circulation. 3. Histamine also is followed by contraction of the intestinal vessels (actually measured as decrease in volume of the intestine) and decrease of the outflow from them. The blood pressure fell, however, in contradistinction to the reaction to the three other drugs. 4. Exclusion of the liver, of the splanchnic region, or of a part or the whole of the nonsplanchnic portions of the systemic circulation did not change essentially the form of the reaction of the peripheral vessels to any one of the

four drugs used. This conclusion is difficult to align with the experiment noted under conclusion 2 since in the intact circulatory system acetylcholine was followed by a fall in arterial pressure.

Some of the results of these studies are interesting because they are contrary to the usual conception of the action of such drugs, as for instance, acetylcholine. Unfortunately, the authors are not clear about the particular type of peripheral vessel (i.e., arteriole, capillary or venule) that they are studying. They accept decrease in outflow from an organ as evidence of increase of peripheral resistance and lightly assume, the evidence being very poor, that there is no storing of blood in the organs. They mention, only to waive, objections such as change in volume of the gut itself to the use of intestinal volume as a record of constriction or of relaxation of the intestinal arterioles. For these reasons, the conclusions appear to need confirmation.

J. M. S.

Sunder-Plassmann, P., and Muller, K.: Raynaud's Disease and the Neurovegetative-Hormone System. Klin. Wchnschr. **16**: 145, 1937.

A well-studied case of Raynaud's disease of the hands in a woman, twenty-seven years of age, is reported. Numbness and blanching had been present for six years; severe attacks of pain, pallor and cyanosis, and thickening of the skin, for three years. Infections of the fingers had been frequent since adolescence and always healed slowly. Diathermy and use of padutin were without effect. On examination typical attacks of Raynaud's disease of the hands were witnessed, and permanent tropic changes were noted. The feet were cold but otherwise normal. Blood sugar was low (59-67 mg. per cent), and after injection of suprarenin the blood sugar curve showed a delayed rise suggestive of adrenal insufficiency. The blood calcium level was high (15.2 and 17.2 mg. per cent). The notion of a parathyroid tumor was entertained. Bilateral injection of the stellate ganglion with novocaine afforded such complete and immediate relief that extirpation of the left stellate ganglion was done. This operation was followed by flushing of both hands but only the left grew warm, and so four days later the right ganglion was removed; removal was followed by relief of symptoms and increase of temperature on the corresponding side. Examination nine months later showed that relief was still complete. More remarkable still were the findings that the level of calcium in the blood had returned to normal (12.5 mg. per cent) and that the rise in blood sugar after suprarenin was less delayed. Pathological changes were found in the excised ganglia. The authors believe that the case supports the idea that Raynaud's disease is of "neurovegetative-hormonal" origin.

J. M. S.

Smithwick, R. H.: The Value of Sympathectomy in the Treatment of Vascular Disease. N. England J. Med. **216**: 141, 1937.

Dorsal and lumbar sympathectomies for relief of arterial spasm in upper and lower extremities respectively are successful when preganglionic section rather than ganglionectomy is performed. Long-standing success from lumbar sympathetic ganglionectomy is attributed to the resultant preganglionic section since the synapses to the vasoconstrictor fibers in the foot lie in the ganglia below, rather than in those customarily excised. Ganglionectomy in the thoracic region has not met with success because it consists in removal of the ganglia concerned in the sympathetic innervation of the hand and results in marked sensitivity of the vessel wall to sympathicomimetic hormones. Preganglionic section of appropriate dorsal sympathetics, while leaving the ganglia intact, leads to satisfactory vasodilatation in the upper extremities.

In angina pectoris painful impulses from the heart pass only to the upper four to six ganglia of the thoracic sympathetic trunk. Excision of the ganglia or section of the rami between these ganglia and the corresponding intercostal nerves is an operation of magnitude, but it will result in complete denervation. Paravertebral alcohol injection, when skillfully done, is equally satisfactory, carries a negligible risk, and results in very little disability. The majority of cases require left-sided injections only. Good results were obtained in all but three of thirty-five cases so treated by J. C. White.

Seven methods of splanchnic sympathectomy for relief of essential hypertension are discussed. In early cases symptomatic improvement and a marked fall in blood pressure resulted from appropriate splanchnic sympathectomy. Considerable improvement resulted in less advantageous cases. It is possible that sympathectomy will defer or even prevent irreversible, sclerotic changes in the vessels.

H. M.

Pearl, Felix: Peripheral Arteries: Their Importance in Industrial Practice. California & West. Med. **46**: 35, 1937.

The important part played by diseases of the peripheral arteries in industrial accidents has not been sufficiently realized in the past. The rôle of the peripheral arteries as related to industrial practice may be divided into two broad phases: (1) direct injuries to previously normal peripheral arteries; (2) industrial accidents occurring in individuals who have chronic arterial disease. The indications for and treatment of peripheral disease in industrial practice are discussed.

E. A. H.

Lindskog, G. E., and Howes, E. L.: Cervical Rib Associated With Aneurysm of the Subclavian Artery. Report of a Case and Review of the Recent Literature. Arch. Surg. **34**: 310, 1937.

A new case of aneurysm of the subclavian artery in association with cervical rib is reported and the literature on the subject which has collected since Halsted's summary in 1916 is reviewed. There is no agreement as to the proper method of treatment in such cases. A study of the cases recorded in the literature reveals that this type of aneurysm does not tend to increase in size nor is there great danger of rupture. It would appear that surgical removal of such aneurysms is dependent upon the presence of complications, such as pressure on the brachial plexus. Recent studies indicate that the vascular deficiency in the affected arm is due to reflex effects on the peripheral arteries from local irritation rather than to the pathologic changes in the artery itself. For this reason, when surgery is done, it would seem that scaleniotomy is preferable to resection of the rib. Such a procedure was carried out with satisfactory results in the case which is reported.

E. A. H.

Silbert, Samuel: Thrombo-Angiitis Obliterans and Addison's Disease in the Same Patient. J. A. M. A. **108**: 551, 1937.

A twenty-year-old white youth was observed intermittently from April, 1935, to May, 1936. He had experienced symptoms of peripheral arterial occlusion for one year, and had developed gangrene in a great toe. The foot healed under treatment in six weeks, but a month later pigmentation, hypotension, weight loss, and chemical studies led to a diagnosis of Addison's disease. There was no clinical evidence of tuberculosis or syphilis. The chest x-ray film showed no evidence of tuberculosis. Administration of adrenal extract was followed by a satisfactory decrease in the

manifestations of Addison's disease. No clear correlation is presented between the administration of adrenal extract and further improvement in the condition of the affected limb.

The question is raised whether the Addison's disease could be due to atrophy of the suprarenal glands secondary to obstruction of their blood supply by vascular disease. The author points out that thrombosis of intraabdominal arteries in patients with thromboangiitis obliterans occurs only when the disease is very far advanced and that occlusion of the arterial blood supply of both adrenal glands has never been reported.

H. M.

Flint, E. R.: An Unusual Vascular Complication of Cervical Rib. Brit. J. Surg. 24: 622, 1937.

A nonpulsating swelling in the right supraclavicular fossa was seen in a patient with bilateral cervical ribs. Operation revealed a thrombosed aneurysm of the subclavian artery lying on a sharp projection of a cervical rib. The aneurysm was excised, and the pain which had been present in the hand disappeared.

H. M.

Uprus, V., Gaylor, J. B., and Carmichael, E. A.: Vasodilation and Vasoconstriction in Response to Warming and Cooling the Body. A Criticism of Methods. Clin. Sc. 2: 301, 1936.

The reliability of skin temperature measurements as an index of vasodilation and vasoconstriction has been studied by determining the response of the skin temperature to warming and cooling of the body in four normal subjects and in two subjects with damaged spinal cords from fracture of the spine. Vasodilation was produced by a heat tent or by the method of Gibbon and Landis, and vasoconstriction was produced by placing the limbs which were not tested in tanks of water at 9° C. to 12° C. after adequate warming had occurred. The rectal temperature was taken by a special thermocouple placed high in the rectum. The rectal temperature recorded in this way is believed to be a suitable index of arterial blood temperature and, in all probability, the temperature of the blood going to the central nervous system. These experiments indicate that in the normal subject the onset of vasodilation is dependent upon the local temperature of the limb, the posture of the limb, and the rapidity of rise of blood temperature. The hot air bath produced only a low gradient of blood temperature rise, whereas, immersion methods gave a rise in blood temperature adequate to overcome local conditions apart from marked changes in posture. The gradient of rise of blood temperature is of importance in both the vasodilation produced by the hot air bath and immersion methods, but the actual temperature of the blood is of importance only when the hot air bath is utilized. If the blood temperature is not rising rapidly, the time of onset of vasodilation in the limbs of the subject should not be accepted as an indication of disturbance of the nervous mechanism.

E. A. H.

Book Reviews

DIE HERZ- UND GEFÄSS- KRANKHEITEN. By Professor Dr. Walter Frey, Direktor der Medizinischen Universitätsklinik, Bern. Berlin, 1936, Julius Springer, 341 pages, 61 figures. Price (paper) RM 29.—; (bound) RM 32.60.

Frey has recently published an interesting volume on diseases of the heart and blood vessels in which he discusses the fundamental background of the various abnormalities of the circulation. The book is essentially one of etiology, pathology, and pathogenesis. Much less attention is paid to the clinical side—that is, to the diagnosis, prognosis, and treatment. Hence the work is much more important as a fundamental survey for the student and practitioner than for clinical reference. It is refreshing to find a volume like this from the Old World based on an etiological classification.

The arrangement of the book is as follows:

I. Embryology (a few pages).

II. Congenital defects and developmental defects, with tables of normal growth, and including a discussion of involution in old age. The author refers in this section of the book to the fact that there is no growth hypertrophy of the heart as such.

III. Indurative lesions, including scleroses and abnormal muscle chemistry.

A. Cardiosclerosis.

1. Aortic sclerosis.
2. Valvular sclerosis (in which too much space is given to mitral sclerosis).
3. Coronary sclerosis (in which the arrhythmias are discussed).

B. Arteriosclerosis.

1. Aorta.
2. Pulmonary arteries.
3. Middle sized vessels.

Under this heading there is a discussion of blood pressure, elasticity of arterial walls (with formulas), pulse pressure and the sphygmogram, pulse size, and heart size and form. There is too much included here.

4. Sclerosis of the visceral arteries (arteriolosclerosis) with a discussion particularly of kidneys, pancreas, and spleen.

C. Phlebosclerosis.

These sections complete about half the book. Then we go on to

IV. Bacterial toxic damage, mostly allergic, with a discussion of

A. General pathogenesis.

1. Leucocyte reaction.
2. Metabolic reaction.
3. Fever.

B. Carditis.

1. Endocarditis, subdivided into the rheumatic, ulcerative, and inactive valve lesions. Rather clumsily under heading *A*, there is a discussion of the treatment of myocardial insufficiency and the application of digitalis, etc.

2. Myocarditis.

a. Parenchymatous, as from diphtheria.
b. Interstitial rheumatic.
c. Embolic bacterial.

3. Pericarditis.

a. Contact pericarditis—dry, with effusion, and adhesive. Here it is of interest to note that the author suggests a trial of diathermy in calcification of the pericardium.

b. Rheumatic, in which Brauer's and the so-called Schmieden's (the Delorme) operation are recommended. It has been the general experience, however, that rheumatic pericarditis does not fit into this category, that is, constrictive pericarditis is practically never the result of rheumatic pericarditis and so this recommendation of therapy is misplaced.

c. Bacterial, embolic.

C. Arteritis.

1. Bacterial.

a. Mycotic.

b. Tuberculous.

c. Syphilitic. This discussion of syphilitic arteritis, including the details of treatment, is one of the most satisfactory sections of the book.

2. Toxic, rheumatic.

a. Periarteritis nodosa.

b. Thromboangiitis obliterans.

D. Phlebitis.

1. Bacterial, embolic.

2. Toxic, a-bacterial, reactive.

V. Endocrine and vegetative nervous affections of the heart function.

A. The so-called dysglandular conditions.

1. Hyperthyrosis (hyperthyroidism).

2. Hypothyrosis (myxedema).

3. The climacterium.

4. Adrenal insufficiency.

B. Neuroses.

1. Constitutional, congenital.

2. Acquired.

The volume closes with a brief index.

This book can be heartily recommended to those who wish to study or to review the fundamental causes of cardiovascular disease, but it cannot be satisfactorily used as a textbook for the diagnosis and treatment of these disorders.

Errata

In the article, "Coronary Thrombosis: An Investigation of Heart Failure and Other Factors in Its Course and Prognosis," by A. M. Master, M.D., S. Dack, M.D., and H. L. Jaffe, M.D., New York, N. Y., appearing on page 330 of the March issue, the following corrections are made:

In Table IV the heading "Slightly Prolonged (12-20 sec.)" should read, "Slightly Prolonged (18-20 sec.)" instead.

On page 340, line 12, "(13 per cent)" should be changed to "(26 per cent)."

In Table XII the last three figures in the last column should read: 42%
60%
16 (42%).